ROLE OF THOMPSON SCORE IN PREDICTING NEURODEVELOPMENTAL OUTCOME

Dissertation submitted to

THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY

In partial fulfilment of the regulations for the award of degree of

M.D DEGREE (PEDIATRICS) BRANCH VII

INSTITUTE OF SOCIAL PEDIATRICS

STANLEY MEDICAL COLLEGE

CHENNAI – 600 001

APRIL 2016

DECLARATION

I, **Dr.B.RUPA**, solemnly declare that the dissertation titled **"ROLE OF THOMPSON SCORE IN PREDICTING NEURODEVELOPMENTAL OUTCOME"**was doneby me at**Government Stanley MedicalCollege during 2013- 2016**under the guidance and supervision of my chief **Prof. SHANTHIM.D, D.C.H.**

The dissertation is submitted to **The Tamil Nadu Dr.M.G.R Medical University** towards the partial fulfilment of the rules and regulations for the **M.D. Degree Examination - BRANCH VII - in Pediatrics**.

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This is to certify that the dissertation titled **"ROLE OF THOMPSON SCORE IN PREDICTING NEURO DEVELOPMENTAL OUTCOME"** is a bonafide research work done under my guidance by **Dr.B.RUPA,** Postgraduate student, Department of Pediatrics, Government Stanley medical college, The Tamil Nadu Dr.M.G.R Medical University, Chennai, in partial fulfilment of the requirement of the award for the degree of **M.D PEDIATRICS - BRANCH VII.**

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ACKNOWLEDGEMENT

It is with immense pleasure and gratitude that I thank **Dr.ISSAC CHRISITIAN MOSES M.D., DEAN, STANLEY MEDICAL COLLEGE** for bestowing me the permission and privilege of presenting this study and for enabling me to avail the institutional facilities.

I am gratefully indebted to **Prof.SHANTHIM.D, DCH**, Director, Department of Pediatrics, Stanley Medical College for her valuable guidance and motivation .

I sincerely thank **Prof.DEVI MEENAKSHI, M.D,**Department of Neonatology,Stanley Medical College for offering guidance and encouragement throughout the study, and for permitting me to avail the lab facilities that has made this study possible.

I am very grateful to both my chiefs, **Prof.ARAVINDM.D, DCH and Prof.LAKSHMIM.D,DCH** for guiding through my dissertation process and providing departmental resources for the conductance of this study.

I am extremely thankful to **Dr.ElangoM.D,DCH** Medical Registrar, for hisvaluable suggestions and guidance during this study.

I express my gratitude to the Assistant Professor of PICU **Dr.EkambaranathM.D** forhis valuable help and guidance for this study.

I sincerely thank my Assistant Professor **Dr.P.VenkateshM.D**for his timely help and support throughout the course of this study.

I thank my Assistant Professor **Dr.RajaM.D, Dr.VinothM.D, Dr.KumarDCH** and **Dr.SankaraNarayanan M.D** for their valuable support.

I express my heartfelt thanks to Late **Dr.V.EzhilSrinivasanM.D** whose words of knowledge and encouragement has stayed with me during this course of study.

I sincerely thank all the patients and their parents who participated in this study.

I thank all the NICU staff nurses for their immense help in conducting this study.

Finally I thank all the post graduates in the Department of Pediatrics in our Stanley Medical College who have helped me through thick and thin. It was an immense pleasure working with all.

CONTENTS

ROLE OF THOMPSON SCORE IN PREDICTING NEURO DEVELOPMENTAL OUTCOME IN NEWBORNS.

Birth asphyxia is a condition of impaired gas exchange occurring during labour leading to progressive hypoxia associated with carbon dioxide retention and significant metabolic acidosis.It is an important cause of perinatal mortality and neurological morbidity,Recently new technologies have become available to determine cerebral damage more accurately and earlier in perinatal course.These include computerized tomography (CT),magnetic resonance imaging(MRI),cerebral function monitoring,cranial ultrasound and Doppler ultrasound of middle cerebral artery.These modalities are not available in many neonatal units ,and certainly not in developing countries.There is a need for a simple but accurate clinical method of predicting outcome.

AIM :To determine the ability of THOMPSON SCORE in newborn infant with HIE within 6 hrs of birth in predicting neurodevelopmental outcome at 9 months of age.

JUSTIFICATION OF STUDY:Simplenon invasive clinical tool to select ideal candidate for neuro protective therapy,to do early intervention like physiotherapy,developmental assessment, occupational therapy,to minimize disability in future,to counsel the parents regarding prognosis early.

STUDY POPULATION:Child born with signs of HIE at birth are my study population.50 in each arm as exposed and unexposed group(including 10% lost to follow up)

Exposed-Thompson score more than 10

Unexposed-Thompson score equal or less than 10

Study period-9 months

Methodology-Term infants of 37 weeks of gestation or more are selected with clinical signs of HIE at birth.

INCLUSION CRITERIA-

BOTH 1 AND 2 SHOULD BE PRESENT

1)INFANTS≥37 WEEKS OF GESTATION ADMITTED IN NICUWITH ANY ONE OF FOLLOWING:

A)APGAR Score<5 at 10 minutes of birth

B)Continued need for resuscitation including endotracheal or mask ventilation at 10 minutes after birth.

C)Acidosis within 60 minutes of birth(umbilical cord,arterial,or cord PH<7)

D)Base deficit>16 mmol/lin umbilical cord or any blood sample within 60 minutes of birth.

2)Altered state of consciousness(lethargy,stupor or coma)atleast one of the following

A)Hypotonia

B)Abnormal reflexes(oculomotor and pupillary abnormality)

C)Absent or weak suck

D)Clinical seizures.

EXCLUSION CRITERIA:

1)Infants> 6hrs of age

2)Major congenital abnormality or syndromes that include brain dysgenesis.

Infants scored by THOMPSON SCORE within 6 hrs of birth and for 7 consecutive days.Infants followed up at 3,6,8 months of age.One cranial ultrasound should be done prior to discharge.Detailed neurological and development assessment will be done every 3rd month.

Table 1. Hypoxic ischaemic encephalopathy score.

Sign	Score 0	1	2	3
Tone	Normal	Hyper	Hypo	Flaccid
LOC	Normal	Hyper alert, stare	Lethargic	Comatose
Fits	None	Infreq $< 3\ d^{-1}$	Frequent>2/day	
Posture	Normal	Fisting, cycling	Strong, distal flexion	Decerebrate
Moro	Normal	Partial	Absent	
Grasp	Normal	Poor	Absent	
Suck	Normal	Poor	Absent ± bites	
Resp.	Normal	Hypervent	Brief apnoea	IPPV (apnoea)
Font'l	Normal	Full, not tense	Tense	
				Total score per day-

It is a clinical tool comprising of a set of clinical signs associated with CNS dysfunction.

It is used to assess status of a child following birth asphyxia.

In scoring system,a score of 0 is normal and maximum score is 22 which signifies worst possible status of HIE.

Infants scoring 1-10 are considered to have mild HIE,11-14 have moderate HIE,15-22 are considered to have severe HIE.

This is modified sarnat scoring system.

Infant neurological assessment should be conducted usingDASI II by paediatrician.

Development activities screening inventory(DASI)II-It is designed for early detection of development delay with special focus on young children with language impairment whose cognitive abilities may not be accurately screened with a tool that requires the child to follow spoken instructions.DASI-II instructions may be either verbal or visual.There are 67 items which can be administered in one or two settings.

Description of scales

DASII scale is a point scale with items arranged in ascending order or age placement for both motor and mental scales.
The items in the two scales are classified into content clusters under different areas of development. There are five clusters of motor items and 10 clusters of mental items.

Motor clusters

I. Neck control
II. Body control
III. Locomotion I (Coordinated movements)
IV. Locomotion II (Skills)
V. Manipulation

Mental clusters

I. Cognizance (Visual)
II. Cognizance (Auditory)
III. Reaching, manipulation and exploring
IV. Memory
V. Social interaction and imitative behavior
VI. Language I (Vocabulary and comprehension)
VII.Understanding of relationship
VIII. Differentiation by use, shapes and movements
IX. Manual dexterity

The content clusters have great utility in clinical practice. They may be used in analyzing the child's performance in each area of development obtaining a profile of development with indication of areas of delay in development.
It helps to plan intervention strategy with referenceto child's strengths and weaknesses. It aids in effective counseling of parents for home based stimulation program.

Differential diagnosis with DASII

It is possible not only to identify delays and areas of delays with DASII but cluster analysis

can also help in differential diagnosis.

A Down’s syndrome baby will have better motor than mental profile.A high functioning autistic child will have almost normal motor profile and relatively low onmental but, especially low on language, social interaction. He is likely to do better on memory,understanding of relationships or form boards.

A cerebral palsy child will score low onmotor items, imitative, skills but better on language development, especially receptive language.He may do poorly on timed items, like manipulation and manual dexterity clusters.A child with low stimulational and early deprivation may show adequate score on motobut lower on mental clusters.

Thus, in trained hands, the DASII is a very comprehensive and effective tool often considered the gold standard for developmentalassessment. It should be an integral part of any developmental clinic where effective intervention is planned.

Points to Remember

• Developmental assessment should be an integral part of NICU (Neonatal intensive care unit)

• Developmental screening be done in all high risk infant as early as 3-6 months of age

• DASII (Developmental assessment scales for Indian infants) is a very effective comprehensive and useful tool which is standardized in Indian babies

ROLE OF THOMPSON SCORE IN PREDICTING NEURODEVELOPMENTAL OUTCOME.

INTRODUCTION

Perinatal asphyxia is a important cause of perinatal mortality and morbidity. .Data from the National Perinatal database suggests that perinatal asphyxia contributes to almost 20% of neonatal death in India[20]. Failure to initiate or sustain respiration after birth is the criteria for the diagnosis of asphyxia by WHO[20] . It is a condition of altered gas transfer in delivery of fetus causes CO2 excess and abnormalities in acid base balance of the newborn. During labour uterine arteries and veins get compressed by pressure causing distruption of flow to placenta. .Uterus gets adequate blood only when it is relaxing in between contractions . There is slight fall in blood PH in healthy fetus and placenta during normal labour. Factors that prolong the normal labour or if adaptations in fetus is not successful then it results in fetal hypoxemia and significant metabolic acidosis .If it prolonged beyond certain period there is excess synthesis of lactic acids and this condition can leads to asphyxia . Excitatory and toxic amino acids accumulate in damaged tissues. Sodium and calcium in the tissues becomes excess results in cytotoxic damage and cerebral edema.In tissues there is excess of free radicals and nitric oxide. Blood flow increases in ductus venosus, ductus arteriosus, and foramen ovale at the same time blood flow through the brain ,heart and adrenals is continued when compared to lungs, liver, kidneys and intestine. Post asphyxial neuronal damage is high in developing countries. Factors that determine perinatal asphyxia comprises of

fetal or umbilical cord pH measurement, intrapartum electronic fetal monitoring ,meconium stained amniotic fluid, APGAR score, hypoxic ischemic encephalopathy, and major organ disorder .New technologies that are useful to know damage in the grey matter and white matter include computerised tomography(CT), magnetic resonance imaging(MRI), cerebral function monitoring, skull ultrasound and Doppler ultrasound of middle cerebral artery. Above said techniques are not used widely in several hospitals, especially in developing countries .So we require a basic tool at the same time accurate clinical method to know the neurodevelopmental outcome in newborns.

REVIEW OF LITERATURE

Neonatal Encephalopathy [16]

Neonatal Encephalopathy (NE) is explained as a group of signs of abnormal neurological function in the first few days of life in the term infants, characterized by abnormalities in tone and reflexes, abnormal level of consciousness and it is usually accompanied by neonatal seizures.

Several important factors can cause neonatal encephalopathy ,the most often it is due to hypoxic-ischaemic insult. In deliveries when evidence of Hypoxic insult is not available other causes of neonatal encephalopathy should be looked for.

Some factors that can leads to NE include:

- infection
- perinatal stroke
- intracranial haemorrhage
- congenital brain malformations
- inborn errors of metabolism
- genetic syndromes

Hypoxic ischemic encephalopathy is the main and most serious adverse event affecting term newborns. Hypoxic ischemic encephalopathy is used to describe

neurological syndrome that is occurring secondary to perinatal asphyxia .It occurs in 1.5 to 2.5 per 1000 live births in developing countries.[6,] Gilstrap et al precisely describe birth asphyxia which occurs at time of birth and it is determined by umbilical artery pH, Apgar score and the newborn neurological status. Depression of the newborn defined by APGAR <3 at 1 and 5 minute and umbilical arterial pH <7.0[19]

Five processes of perinatal asphyxia include:

1. Interuption of umbilical circulation
2. Inadequate blood flow to placenta on the maternal side
3. Gas exchange abnormalities in the placenta.
4. Inability of the newborn to maintain lung inflation and problem in moving from fetal to adult circulation.
5. Altered maternal oxygenation

World Health Oragnization	Failure to initiate and sustain breathing
NNPD Network	• Moderate PA: Slow/gasping breathing or an Apgar score of 4 to 6 at 1 minute • Severe PA: No breathing or an Apgar score of 0-3 at 1 minute of age
American Academy of Pediatrics and American College of Obstetrics and Gynecology	Presence of all of following criteria: • Profound metabolic or mixed acidemia (pH< 7.00) in umbilical cord blood • Persistence of low Apgar scores less than 3 for more than 5 minutes • Signs of neonatal neurologic dysfunction (e.g., seizures, encephalopathy, tone abnormalities) • Evidence of multiple organ involvement (such as that of kidneys, lungs

Newborns response to asphyxia in two manners

1. Centralization of fetal circulation with excess flow to adrenals, heart and brain

2. Process of Erythropoiesis becomes more with the excess of immature RBC in peripheral veins. This is responsible for excess of nucleated RBC following perinatal asphyxia.

CIRCUMSTANCES THAT DETERMINES CNS INSULT:

- Cellular susceptibility(neurons most susceptible)
- Vascular territories(Water shed areas)
- Regional susceptibility(areas of higher metabolic rates i.e,Thalamus)
- Degree of asphyxia

ETIOLOGY[2]

.It mainly occurs when cerebral perfusion is so less so that O2 extraction cannot be done from the venous and arterial circulation. As a result oxidative metabolism and cerebral blood flow mis match with each other. The multiple factors that can leads to HIE are

- Include maternal hypotensive states, infertility in the mother,,thyroid disease.
- Intrapartum risk factors include maternal fever, breech presentation, difficult forceps delivery, abruption placenta or cord prolapse.

- ❖ Post natal factors such that sepsis, shock, congenital heart disease and severe respiratory distress

EVOLUTION OF HIE CHANGES[20].

It is slow ongoing mechanism which starts from the injury phase and can extend and can continue after resuscitation phase. At first, insult to the brain is because of ischemia and further injury is because of reperfusion. Penumbra is the region around the infarcted zone . Penumbra zone will continue to reveal features of apoptosis and necrosis once hypoxic insult finishes . PERIOD OF DELAYED NEURONAL INJURY is not understood but extend from 24 - 48 hours then start to resolve.

Additional factors that influence outcome are nutritional status of brain, severe intrauterine infection, pre-existing brain pathology, and frequent seizure disorder[20].

Hypoxic ischemic encephalopathy

It result from a hypoxic process that takes place during the periods of prenatal, intrapartum and postnatal time period.[6] Death, disabilities like seizures developmental delay and cerebral palsy is the outcome in 60% on newborns born with hypoxic ischemic encephalopathy. Majority of underlying events of HIE due to impaired supply of O2 to the brain and it due to reduced supply of blood to brain.

PATHOLOGY OF INJURY

Insults could be of many varieties and it based on time and extend of the injury..

1) GLOBAL ISCHEMIA

Global ischemia occurs when oxygen requirements for cerebral metabolism are unable to met by cerebral perfusion pressure or due to decrease in cerebral arterial or an increase in cerebral venous pressure .

The duration of the insult is inversely proportional to the gestational age of the fetus . The latent period vary from hours to days and is determined by various factors like vascular,cellular and metabolic factors.

FOCAL OR PARTIAL ISCHEMIA

It occurs when artery or venous supply to a region is compromised. The injured region typically consists of central dense region of ischemia that undergoes rapid cell death and the core surrounded by a region of evolving cell injury called penumbra .The cells in the penumbral region initially sustained by anaerobic glycolysis. If the injury is sustained penumbra is transformed in to region of infarction .This period of delay in cell death provides an opportunity for therapeutic intervention.

2) Partial asphyxia with normal acid base balance is due to hypotensives states in mother ,due to decrease in exchange of gases in placenta,and reduced placental

blood flow.This leads to extensive cortical necrosis or posterior parietal parasaggital injury.

3) Partial asphyxia associated with acid base abnormalities leads to injury to white matter. Systolic BP maintain blood flow to the brain. It maintains the blood supply by dilates the arteries to the brain structures..Basal ganglia,thalamus and brain stem nuclei are susceptible to injury due to either excess myelination and excess of glutaminergic synapses.

VARIOUS TYPES OF NEUROLOGICAL INJURY

- Parasaggital lesions
- Status marmoratus
- Focal or multifocal necrosis
- Spinal cord ischemic infarction
- Periventricular leukomalacia

SELECTIVE NEURONAL NECROSIS

LONGER THE INJURY-Involves cortical and subcortical areas

SHORTER THE INJURY-Involves thalamu,basal ganglia and brain stem.

Posterior parietal-occipital region is more prone to injury than anterior cortical areas.

- CORTICAL INJURY-Seizures
- BASAL GANGLIA AND THALAMUS-Irritability, posturing, and brain stem dysfunction.

PARASAGITTAL INJURY-CLINICAL FEATURES

- Weakness and hypotonia in the upper trunk

STATUS MARMORATUS

It refers to characteristic picture of a marble in cerebral cortex and basal ganglia and thalamus.It is commonly associated with choreo athetoid cerebral palsy in children.

FOCAL CEREBRAL NECROSIS

It results from a area of infarcted zone secondary to thrombus or embolus.. Main factors which predisposes this condition are increased platelet count, ITP, vascular malformation, and if the mother uses excess cocaine.

PERIVENTRICULAR LEUKOMALACIA

In preterm babies it involves predominately white matter and results in extensive injury to that areas. Focal necrosis and development of cyst and extensive injury to precursors of oligodendrites is the characteristic feature of periventricular leukomalacia..

OUTCOME is mostly in the form of spastic diplegic cerebral palsy and motor deficit.

RISK FACTORS FOR PERIVENTRICULAR LEUKOMALACIA

- Seizures
- Sepsis
- Recurrent episodes of apnea
- Asphyxia
- Prolonged ventilation

PATHOGENESIS.

It is divided in to four phases

1) membrane depolarization due to fall in energy in grey matter.

2) Pouring of Neurotransmitters and causes extensive injury to the neurons

3) A period of reperfusion

4) A final phase of irreversible cell death.

PHASES OF INJURY DURING REPERFUSION

- FIRST PHASE
  - Cerebral energy metabolism restored over 30 minutes
  - Resolution of acute cellular hypoxic depolarization and cell swelling.
- LATENT PHASE
  - Near normal oxidative cerebral metabolism
  - Depressed electroencephalogram and reduced blood flow.
- SEONDARY ENERGY FAILURE
  - Inhibition of oxidative phosphorylation
  - Cytotoxic edema leading to delayed seizures.

PHASE OF REPERFUSION

This period extends from 6 hours to 15 hours before cell death and provide an opportunity of therapeutic window. This phase is characterized by reduced blood supply to the brain and Electroencephalogram activity is reduced..This phase occurs during the return of blood flow and adequate O2 supply to the brain.

PHASE OF IRREVERSIBLE CELL DEATH

This process results in two different types of death in the brain celli.e Apoptosis and Necrosis

- APOPTOSIS-It is due to shrinkage of nucleus,,condensed forms of chromatin and disintegration of DNA .It occurs due to chronic cellular injury.
- NECROSIS-It is due to cellular swelling, plasma membrane disintegration, extensive inflammation in the cells.

The pathophysiology of HIE is primary energy failure and other one is secondary energy failure.

PRIMARY ENERGY FAILURE:

Decreased in blood supply to white and grey matters in the brain causes fall in O2 and glucose levels in brain leads to excess lactate content and reduced ATP in the brain. This leads to Na-K pump failure and accumulation of Na inside the cells. This mechanism fails to maintain Ca levels inside the cells. This results in increased amounts of glutamate. Necrosis and apoptosis results from ischemia, damage in the

blood vessels, and edema inside the cells. If the hypoxia is very severe , results in ischemic necrosis.

Cell begins to increase in size and resulting in rupture leading to death of the cells. There is additional influx of inflammatory mediators produced by microglial cells. Resulting inflammation .causes scar formation.

Functions of the brain cells decreased due to apoptosis and necrosis. Death occurs to the neuronal cells if ischemia is so severe and it is through necrosis of brain cells

There is period of recovery occurs once the blood flow is returned. This phase is called as latent period of cell death. Optimum time for therapeutic intervention is determined by the latent period. Extensive the insult shorter is the latent period.

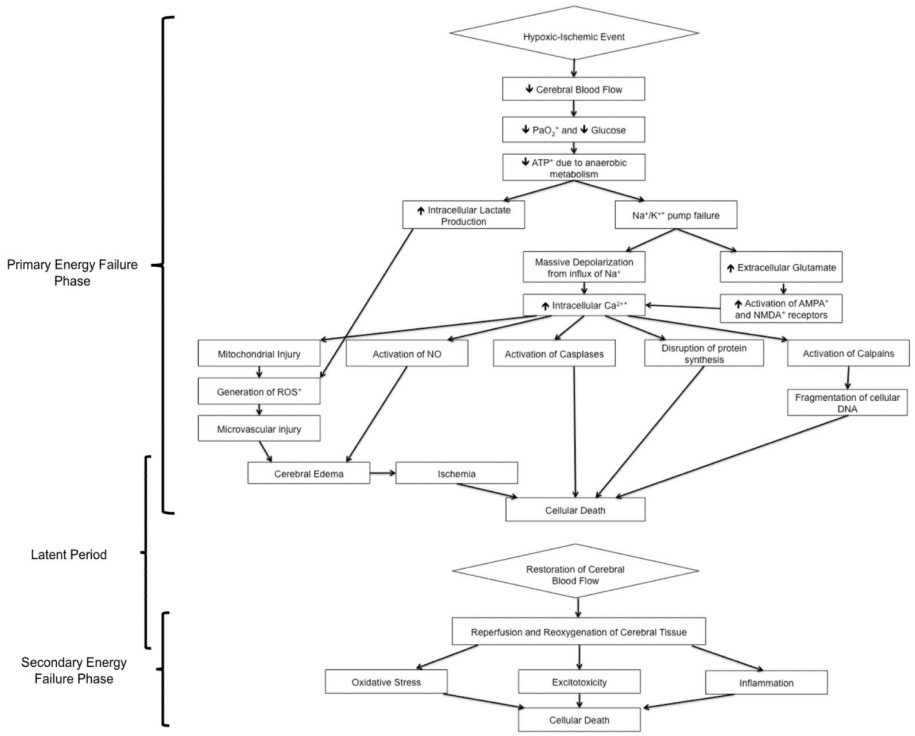

FIGURE 1.PATHOPHYSIOLOGY OF HYPOXIC ISHCHEMIC ENCEPHALOPATHY

v* = increased; = decreased; PaO2 = arterial oxygen; Na+ = sodium;

K+ = potassium;

ATP = adenosine triphosphate; Ca2+ = calcium; NMDA = *N*-methyl-D-aspartate; AMPA =∝-amino-3-hydroxy-5-methyl-4-isoxazoleproprionic acid; ROS = reactive oxygen species;

NO = nitric oxide; DNA = deoxyribonucleic acid.

- The brain is main control centre of the body. It is made up of nerve cells (neurons) that carry messages to and from the body.

- Neurons receive messages from the body with every activity..

- They also send messages to the body to do things like control muscles and movement .When these cells are damaged, the brain may not be able to receive and process information from the body, or send messages to parts of the body.

- Based on the functions of neurons the brain is divided into different areas. Some areas involve muscle control , while other areas are related to vision and hearing. **Depending on the area affected by the lack of oxygen, neonate will have difficulties with the activities controlled by that specific area**.

There are many possible areas of brain that may have been affected. However, the most common areas are the cerebral cortex, basal ganglia ,brainstem and thalamus..

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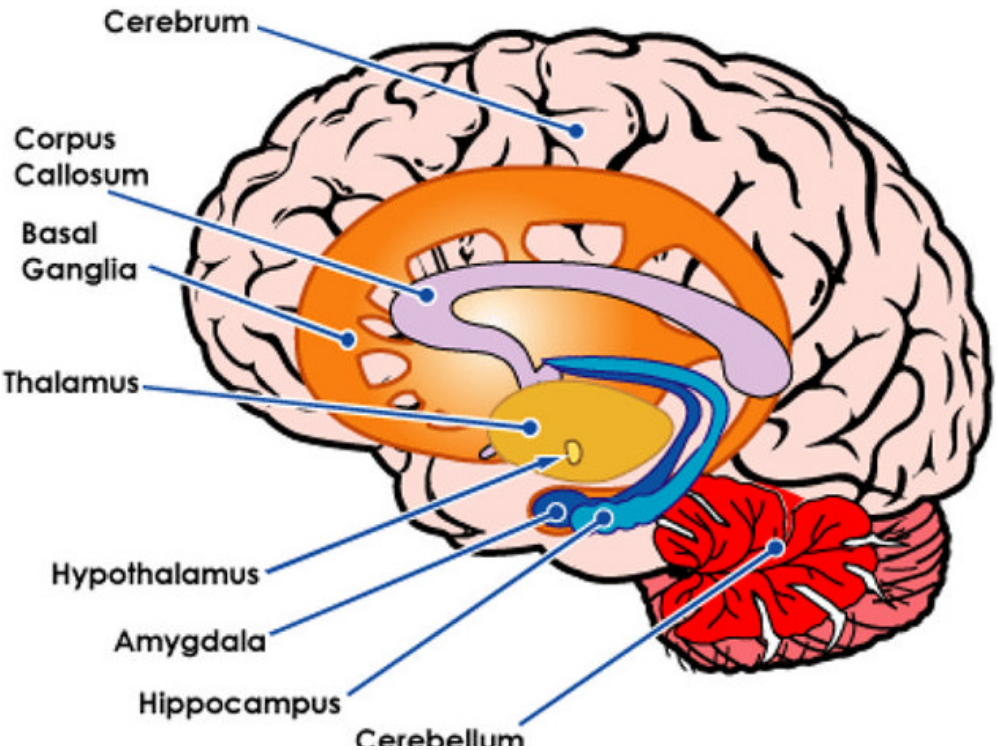


FIGURE 2.LOCATION OF BRAIN STRUCTURES IMPACTED BY TREATMENTS

CNS STRUCTURES SUSCEPTIBLE TO ISCHEMIC INJURY DEPENDS ON THE GESTATIONAL AGE

- For babies <20 weeks-Insults leads to neuronal heterotopia
- For babies 26-36 weeks-Insults mainly affects white matter leading to periventricular leukomalacia.
- For term newborns-Insults primarily affects grey matter

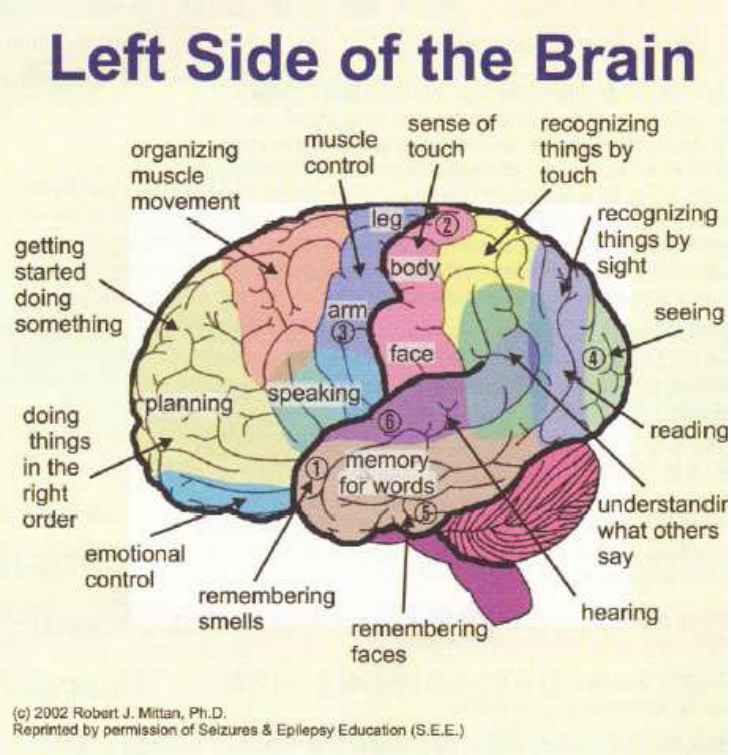


FIGURE -3

Secondary Energy Failure

This process results 6 hours to 48 hours after primary energy failure. The exact mechanisms remain unknown[12] but it occurs due to oxidative stress, excitotoxicity, and inflammatory process. Excess free radicals causes disintegration of cell membranes of the neurons which results in apoptosis and necrosis. This process is called as oxidative stress.

This stress is harmful to neonatal brain and its structures because antioxidants levels in neonatal brain is too low and because it utilizes more oxygen when a transition occurs from fetal to neonatal life. In the neonatal brain free iron is responsible for the formation of free radicals.

Another important cause of injury is due to release of excitatory neurotransmitters namely glutamate which in turn stimulate excitatory receptors results in influx of Na and Ca into the cells.

Glutamate a excitatory neurotransmitter is a predominant neurotransmitter in pathways like vision, hearing and intellect, results in abnormalities in conduction of these pathways in HIE.

Inflammation mediated brain injury also occurs in Hypoxic ischemic encephalopathy. Supportive treatment of HIE is management of seizures and cardiopulmonary support.

CLINICAL FEATURES:[2]

Clinical signs and symptoms depends on timing, duration and severity of insult. Consider infant gestational age while looking for clinical features. Symptoms evolve over a period of 72 hours. Cerebral hemisphere depression is responsible for signs and symptoms in first 12 hours of life although sign of brainstem involvement is there.

Infant is not easily arousable during this period .Involvement of reticular activating system, brain stem and thalamus results in alteration of consciousness.

Hypotonia jitteriness, seizures in the first 12 hours of birth due to extensive involvement of cortex.. Seizures in first 2 to 3 hours indicate severe asphyxia.

Seizures in term infants is usually focal. Subtle seizures is characterized by movements of the eyeballs like conjugate deviation of eyes, blinking or constant opening of eyes.

There is apparent increase level in alertness during 12 to 24 hr after injury but it is improvement of neurological function is not apparent in this period.. Seizures, apnea and jitteriness accompany this period. Deep tendon reflexes and moro reflexes are exaggerated there is weakness in proximal limbs

especially consciousness levels. The clinical condition of newborn comes down beyond 24 -48 hours. Sometimes outcome is so severe that leads to death ,absent DEM ,poor suck and diminished tone and proximal muscle weakness.

When a neonate suffer asphyxia during labour, some of them develop HIE with outcome ranging from complete recovery to death.

Convulsion in the newborns mostly caused by the hypoxic ischemic encephalopathy. But it can be due to antenatal, intrapartum and postnatal causes. Postnatal factors that leads to seizures account for 10% of the cases.

HIE can be suspected in any newborn born but to confirm HIE biochemical parameters are necessary. It includes four main and important features

As suggested by AMERICAN COLLEGE OF OBSTETRICS AND GYNECOLOGY.

These main cardinal features are

- Umblical cord blood pH <7 with profound metabolic or mixed academia
- Apgar <3 after five minutes of birth
- Neurological sequelae like convulsions, coma and decreased tone of newborn.
- MODS(Significant hematological, cardiovascular., gastrointestinal dysfunction)

CLINICAL STAGING OF HYPOXIC ISCHEMIC ENCEPHALOPATHY

FACTORS	STAGE1	STAGE2	STAGE3
LEVEL OF CONSCIOUSNESS	ALERT	LETHARGY	COMA
MUSCLE TONE	NORMAL	HYPOTONIA	FLACCIDITY
TENDON REFLEXES	NORMAL/ INCREASED	INCREASED	DEPRESSED/ ABSENT
MYOCLONUS	PRESENT	PRESENT	ABSENT
SUCKING	ACTIVE	WEAK	ABSENT

MORO	EXAGGERATED	INCOMPLETE	AB SENT
GRASPING	NORMAL	EXAGGERATED	ABSENT
OCCULOCEPHALIC	NORMAL	OVERACTIVE	REDUCED

Differential Diagnosis of Neonatal Seizures*
Metabolic

Hypoxia-ischemia (i.e., asphyxia) **Hypoglycemia** **Hypocalcemia** **Hypomagnesemia** **Hypoglycemia** **Glycogen storage disease** **Galactosemia**	**Intracranial hemorrhage** **Subarachnoid hemorrhage** **Subdural/epidural hematoma** **Intraventricular hemorrhage**
Cerebrovascular lesions (other than trauma) Cerebral infarction (thrombotic vs. embolic causes) Ischemic vs. hemorrhagic lesions Cortical vein thrombosis Circulatory disturbances from hypoperfusion	

Idiopathic

Hypomagnesemia Infant of a diabetic mother Neonatal hypoparathyroidism Maternal hyperparathyroidism High phosphate load Other electrolyte imbalances Hypernatremia Hyponatremia	**Cerebrovascular lesions** (other than trauma) Cerebral infarction (thrombotic vs. embolic causes) Ischemic vs. hemorrhagic lesions cortial vein thrombosis circulatory disturbances from hypoperfusion
Infections Bacterial meningitis Viral encephalitis Congenital infections Herpes simplex Syphilis Cytomegalovirus infection	**Drug withdrawal or toxins** Prenatal exposure to substances of abuse—methadone, heroin, barbiturate, cocaine Prescribed medications— propoxyphene, isoniazid Local anesthetics

Coxsackie virus meningoencephalitis Toxoplasmosis Acquired immunodeficiency syndrome (AIDS) Brain abscess	
Familial seizures Neurocutaneous syndromes Tuberous sclerosis Incontinentia pigmenti Autosomal dominant neonatal seizures	**Amino acid metabolism** Branched-chain amino acidopathies Urea cycle abnormalities Nonketotic hyperglycinemia Ketotic hyperglycinemia
Brain anomalies (i.e., cerebral dysgenesis from either congenital or acquired causes) Hypertensive encephalopathy Selected genetic syndromes Zellweger syndrome Neonatal adrenoleukodystrophy Smith-Lemli-Opitz syndrome	

HIE can be classified as mild, moderate and severe based on clinical features

- In mild HIE, infant is hyper alert, uninhibited reflexes and sympathetic over activity.
- Moderate HIE is characterized by depressed reflexes, hypotonia , seizures, stupor and lethargy.
- .In severe HIE there is coma , hypotonia, suppressed brain stem function ,seizures and increased intracranial pressure.

Severity of HIE in a newborn can be assessed by classification given by Levene. Cerebral lesions characterized by seizures, mental retardation and motor deficits. Basal ganglia lesion characterized by choreo -athetosis and rigidity. The lesion in the basal ganglia is characteristically called as status marmoratus. Extra pyramidal abnormalities appear late often later than one year. Spastic diplegia mostly involving lower limbs than upperlimbs in premature born infants causing motor deficits resulting neurological sequale is periventricular leukomalacia. Diagnosis of cerebral palsy should be done at earliest so that we can institute therapy earlier.

HIE:[18]The Sarnat and Sarnat classification identifies 3 levels or grades of severity of

- GRADE 1(MILD) HIE: Characterized by active tendon reflexes hyperalertness, mydriasis, jiterriness, but they don't have seizure. Majority of such babies may have normal neurological outcome.

- GRADE 2(MODERATE) HIE: Characterized by lethargy, poor feeding, decreased primitive reflexes, hypotonia, seizures and miosis. Such babies have 25-45% risk of death or significant disability.

- GRADE3 (SEVERE) HIE: Characterized by stupor, coma, marked hypotonia with intermittent decorticate posturing, irregular respiration, and absent primitive reflexes. Newborns in this have 90% chances of death or more severe neurological sequele.

- Durations of symptoms in mild HIE is less than 24 hours,and in moderate HIE IS 2 TO 14 days and in severe HIE it is hours to weeks.

- Outcome-MILD HIE-About 100% normal outcome

MODERATE HIE-80% HAVE NORMAL OUTCOME,ABNORMAL ONLY IF SYMPTOMS PRESENT MORE THAN FIVE TO SEVEN DAYS.

SEVERE HIE- DEATH 50% OF NEWBORN ,50% OF NEWBORNS HAVE SEVERE NEUROLOGICAL SEQUELAE.

Apgar score will not predict outcome in newborn born with HIE. However predictive value increases if Apgar is continues to be in low values. Neurological abnormalities three times more common if the Apgar is less than 6 at five minutes of birth.

- Incidence of long term complications in mild HIE is low
- In moderate HIE 20 to 40% chances of abnormal outcome
- In severe HIE outcome is usually death within first few days after birth or newborn have neurological deficit .

Depressed primitive reflexes with hypotonia and respiratory problems in the form of apnea indicates poor outcome in newborns with HIE.

CLINICAL FEATURES OF SEVERE HIE IN TIME FRAME[20]

Birth to 12 hours	Depressed level of alertness, periodic breathing or respiratory failure, intact pupillary and occulomotor responses, hypotonia, seizures
12 to 24 hours	Variable change in level of alertness, more seizures, apnoeic spells, jitteriness, weakness in upper and lower limbs, upper>lower (full term), hemiparesis (full term), legs (premature)
24 to 72 hours	Stupor or coma, respiratory arrest, brain stem pupillary and occulomotor disturbances, catastrophic deterioration with severe intra ventricular hemorrhage and periventricular hemorrhagic infarction (premature)
After 72 hours	Abnormal suck reflexes, swallowing, gag and abnormal tongue movements, diminished tone in limbs, weakness in proximal limbs, upper>lower (full term), hemiparesis (full term), lower limbs or hemiparesis (premature),stupor

CLASSIFICATION OF HIE BASED ON LEVENE STAGING[20]

	Mild	**Moderate**	**Severe**
Consciousness	Irritable	Lethargy	Comatose
Tone	Hypotonia	Marked hypotonia	Severe hypotonia
Seizures	No	Yes	Prolonged
Sucking/respiration	Poor suck	Unable to suck	Unable to sustain spontaneous respiration

RADIOLOGICAL FEATURES:

In term infants blood flow is ventriculofugal and changes are mainly in watershed border zones namely parasaggital grey matter and subcortical white matter .Severe HIE in term babies results in basal ganglia ,thalamic as well as sensorimotor cortex (perirolandic region) injury.

PATTERNS OF NEONATAL ISCHAEMIC BRAIN INJURY:

- IN LESS THAN 28 WEEKS-

  Hydrancephaly and porencephaly and immature brain not able to react with gliosis and liquefied brain parenchymal defect and enlargement of CSF spaces.

- PERIVENTRICULAR-INTRAVENTRICULAR HAEMORRHAGE

  Occur usually between 28 to 32 weeks and starts from the germinal matrix zone of sub ependymal regions It is a important zone in a newborn which is capable of producing cells ,neurons and glial cells in the fetus.. Prematurity and number of capillaries has a direct correlation.

- SUBCORTICAL LEUKOMALACIA AND PERIVENTRICULAR LEUKOMALACIA:

  Occurs usually between 32 and 36 weeks.Pathology behind this is extensive coagulation necrosis of the white matter on either sides.results in the formation of cavity lateral to the lateral ventricles and reduced myelination of the nerve fibres and extensive white matter loss. Both are a continuous disease spectrum, vascular border zones shift toward periphery brain matures further.. For this reason, White matter lesions move from periphery to subcortical zone.

- HYPOXIC ISCHAEMIC ENCEPHALOPATHY OF THE TERM NEWBORN:

  If the hypoxic ischemia is more severe multicystic encephalomalacia results .If hypoxic ischemia is less severe lesions common in high oxygen demand areas such as deep grey matter..

HIE SCORE

Neurological status of a newborn can be predicted by this score.

Numerous scoring systems have been used in various studies. Portmann found a score to assess morbidity and mortality in earlier days of life. The most widely used scoring system for the infants with HIE is sarnat and sarnat.. MILD,MODERATE AND SEVERE Groups. To classify the newborn into three types is so difficult in this staging system. Outcome of the newborn in moderate group is also unpredictable..

However scoring system needs EEG and other laboratory values is unavailable in our hospital setup.

Scoring system used by Thompson is numeric and it also includes lesser variables. It is much simpler and it is based on Sarnat and Sarnat scoring system. The score consists of nine signs namely, level of consciousness, posture ,tone, reflexes(Moro, sucking ,grasp) seizures, respiration and based on anterior fontanel tension.

Score of each sign range from 0 to 3 and total score for each day is documented.

More severely affected infant will have highest score. 22 is the highest score of newborn .It cannot be applicable in paralyzed newborns.In newborns who are on ventilators it is applicable equally.

COMPONENTS OF THE HIE SCORE:

- Tone

  The tone progresses from normal and slightly increased peripheral tone in the mildly affected infant. The more severely affected infant is generally hypotonic or completely flaccid.

- Level of consciousness (LOC)

  The mildly affected infant has a normal LOC or is hyper alert and staring. There may be normal or decreased spontaneous movement and exaggerated responses to minimal stimuli. The more seve ely affected infant progresses through lethargy to complete unresponsiveness.

- Fits (clinically apparent seizures)

  The score increases with increasing frequency of seizures.

- Posture

  In this study an intermediate score of 1 is given to the neonate who has mild to moderate HIE. The neonate may show intermittent bicycling movements of the limbs together with fisting (thumbs flexed, adducted and opposed across the palms).

- Primitive reflexes: Moro, palmar grasp and sucking reflex

  These reflexes are normal in the mildly affected infant, poor or partial in moderate HIE and absent in severe HIE.

- Respiratory pattern

  In mild HIE the infant breathes normally or hyperventilates. More severely affected infants have episodes of apnoea and may require ventilation.

- Fontanel tension.

  The severely affected infant may have a full or tense (bulging) fontanel.

From the previous studies it was known that positive predictive values of Thompson score for predicting poor outcome in moderate and severe HIE is 90% and 100% respectively and negative predictive value for the scoring system was 81.4% sekala D et al.

C Thompson et all stated that sensitivity and specificity Thompson score in predicting neurodevelopmental outcome is 100% and 93% respectively.

Alon R Horn et all stated that Thompson score has 100% sensitivity and 61% specificity in predicting neurodevelopmental outcome.

Wilkinson et all stated that Sarnat staging has sensitivity of 100% and specificity of 93% in predicting outcome.

Boubou Hallberg et all stated that at one year of age Thompson score has high predictive value of 92% with a peak score of 15 and above and negative predictive value of 82% for abnormal outcome. This score has widely introduced because it predicts neurological outcome during first hours of life as compared to sarnat score, which is reliable after 24 hours.

C Thompson et all stated that positive predictive value and negative predictive value for initial HIE score more than 10 in predicting neurodevelopmental outcome was 65% and 100 % respectively and sensitivity and specificity was 100% and 61% respectively.

Other studies used clinical grading system to predict neurological outcome like post asphyxial score of Lipper which uses 17 items which will predict as early as 24 hours .Another system used was Bao assessment but it requires a training course of 2 weeks.

Robert and finer proposed perinatal factors to predict neurological outcome in moderate encephalopathy group and suggest that newborns can be discharged at an early age from follow up.

Cerebral Function Monitoring [16]

It is used to document electrical activity of the brain in the form of Electroencephalogram . Global or hemispheric electrical activity is provided by a EEG .It can single or dual time compressed and filtered electroencephalogram. However it is not easily accessible in developing countries.

Document electroencephalogram before giving phenobarbitone but if the EEG is not accessible treatment should not be delayed.

ULTRASOUND SCAN OF THE SKULL

Many newborn conditions can mimic like Hypoxic ischemic encephalopathy and these conditions should be ruled out before starting cooling therapy. Ultrasound scan should be done to know the resistance index.

Resistance Index

It is usually done in newborns with suspected HIE and it is done in first few days of life. If the value of resistance index is less than 0.55 it is usually associated with poor prognosis. It indicates abnormal blood flow to the brain most probably dilatation of blood vessels of the brain

HIE findings in cranial ultrasound:

1. generalised increase in echogenicity, indistinct sulci and narrow ventricles usually denotes cerebral edema
2. More echogenicity of thalami and parenchymal echo densities in the first few days of life.
3. (Resistive Index <0.55) in anterior cerebral artery indicates adverse prognosis

4. When there is increased velocity of blood flow in the end diastole when compared with systolic flow of blood predicts poor prognosis.

Magnetic Resonance Imaging (MRI)

Abnormalities are well seen on T1-weighted magnetic resonance image

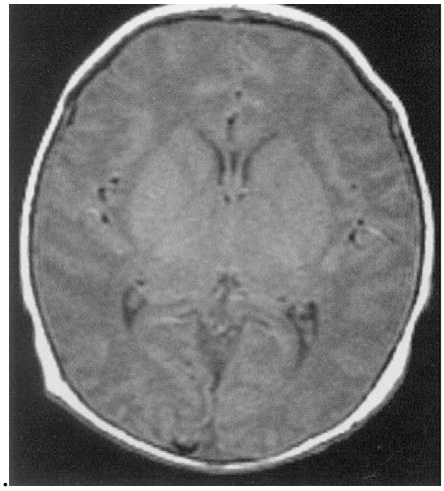
- It is mainly used to confirm HYPOXIC ISCHEMIC ENCEPHALOPATHY and assess the outcome in newborns
- It cannot diagnose injury level when done in the first few days of life
- It is usually done in first few days of life when intraventricular hemorrhage being suspected.

- Diagnosis and outcome of the newborn can be assessed in newborns with HIE when done in tenth day of life.

- In conditions like abruption placenta MRI findings are thalamus and basal ganglia lesions and posterior limb of internal capsule abnormalities

- PLIC is associated with poor prognosis.

- Cortex lesions are more common with prolonged duration of hypoxia.



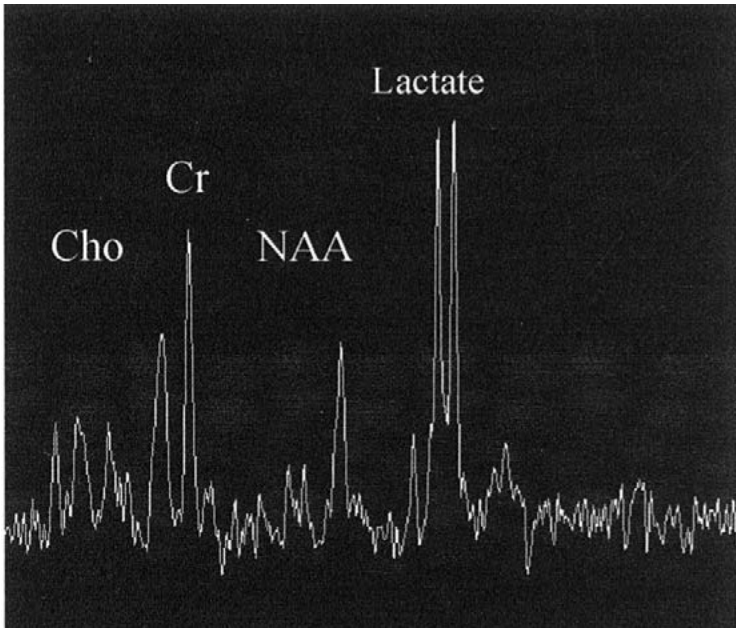
MR image shows loss of signal intensity in the posterior limb of the internal Capsule.

MAGNETIC RESONANCE SPECROSCOPY

Magnetic Resonance Spectroscopy.

- Magnetic resonance spectroscopy findings predicts accurate progonosis.

- if is abnormal it indicates poor prognosis.
- It accurately predicts cognitive and neurological outcome.
- Chronic insults to brain results in the formation of lactate and N-acetyl aspartate in the brain
- When glucose metabolized anaerobically results in the production of lactate levels in the first day and increased persistently remain high after 24 hours
- N-acetyl aspartate will not come down to normal levels after 48 hours
- N-acetyl aspartate start to decrease but exact duration is unknown Magnetic resonance spectroscopy can very well predicts convulsions in newborn and predict metabolic abnormalities in newborn than doing imaging studies like MRI and CT scans.



The MR spectra show elevated lactate and decreased *N*-acetyl aspartate (NAA) peaks in the basal ganglia in that area CT SCAN[17]:It cannot diagnose grey matter lesions when compared to MAGNETIC RESONANCE IMAGING

TREATMENT:

1) Whole body hypothermia

2) Maintain normal blood glucose.

3) Maintain normal blood pressure.

4) prevent or control seizures

5) prevent or minimize cerebral edema.

Stabilisation of babies post-resuscitation and initial management where there is a risk of or diagnosed HIE [18]

Initial management[20]

Transfer the baby to special care newborn unit.

Arterial blood gas analysis should be done in all babies with HIE. Those babies with respiratory difficulties needs to be admitted in neonatal intensive care

unit and should be monitored intensively. Newborns with mild HIE transferred to mothers. Frequent monitoring is needed in these infants. Severe asphyxiated infants need to be transferred to NICU.

Maintain temperature

Thoroughly dry the newborn and place the newborn in the warmer.. Adverse outcome can occur due to hypothermia or hyperthermia. Metabolic demands of the newborn will be excess if the newborn develops hypothermia. It will add some stress to newborn .This excess stress will cause problems like acid base abnormalities. reduced blood pressure, cardiac arrest and pulmonary hemorrhage.

Urgent requirements for airway, ventilation and circulatory support are assessed and managed

- Intubate and ventilate if the spontaneous breaths are inadequate, desaturation despite oxygen, blood gases shows respiratory failure, features of obtundation, or early occurrence of seizures

- Volume replacement indicated where there is suspected blood loss, poor perfusion, hypotension.

Monitor glucose levels in the blood and packed cell volume and arterial blood gas analysis. Utmost importance should be given to maintain hyperoxia, hypocarbia and hyperglycemia in first 48-72 hours because these will cause irreversible injury to the newborn grey matter and white matter which is already injured.

Respiratory

- Monitor oxygen saturations with a pre-ductal target of 90 – 95 %
- In ventilated babies maintain pCO2 at 35-45 where possible.
- Many babies with HIE will spontaneously hyperventilate
- Maintain pH7.35-7.45.

Cardiac

- Attach cardiac monitoring
- Monitor non-invasive blood pressure where arterial access is not available. Normal mean arterial BP should be > 40. Pending arterial line placement,15 minutely Doppler measurement must be recorded
- A baseline bradycardia (80 – 100) is common with hypothermia, therefore adjust the low alarm to 80 bpm.
- Hypotension is a common sequale of myocardial ischemia
- If hypovolumia is suspected give 10–20 mL/kg of 0.9% sodium chloride. Inotrope therapy may also be needed

Fluids and electrolytes

- Insert a nasogastric tube and keep this on free drainage. Do not feed because of risks of ischemia of gut and airway compromise
- Insert an IV
- Don't give excess fluids
- Check plasma glucose level and maintain it above 3.5 mmol/L
- Fluid restriction is essential because of the risks of syndrome of inappropriate of antidiuretic hormone secretion and renal failure.

- Glucose infusion rate should be approximately 4 mg/kg/min of 10 % glucose. To avoid hypoglycemia, higher glucose concentrations are required.

- Monitor urine output via weighed nappies

- Take baseline electrolytes and ionised calcium

Neurological

- Perform a complete neurological examination to determine the presence and severity of HIE

- Treat all clinically evident seizures with phenobarbitone.

Initially 20 mg/kg/dose increased up to 40 mg/kg (total) over the first 24 hours

- Seizures due to HIE are often refractory to treatment

- Hypermetabolic cell death can occur due to seizure activity**.** ***Treatment***[20]

A)ADEQUATE VENTILATORY SUPPORT

- Babies with respiratory distress and respiratory failure needs to intubated and connected to ventilator support.
- Some babies born with apnea .It is essential to intubate those babies in labour room and connected to ventilator when shifted to neonatal intensive care units
- Monitor arterial blood gas analysis if it shows hypoxia persisting it is essential to give ventilator support to those babies.
- Maintain spo2 between 90 to 93% in preterm babies
- Those babies with spontaneous breathing give oxygen through hood

B) **MAINTAIN PERFUSION**

- Dopamine and dobutamine should be initiated once babies develops features of shock.
- Monitor urine output continuously
- To assess the perfusion use parameters like blood pressure ,CRT, ABG.
- Perfusion is most important to be monitored in newborns with HIE.

C) VOLUME EXPANSION

Normal saline and RL is most commonly used fluids to maintain intravascular volume.

D) VASOPRESSORS

- 3-5 microgram/kg/min is the ususal dose of dopamine
- Increase the dose upto 10 microgram/kg/min in stepwise manner.
- It can be reached upto 20 if the features of shock still persisting.
- 5microgram/kg/min is the usual starting dose of dobutamines

E)MAINTAIN NORMAL BLOOD GLUCOSE

- Increased blood glucose levels in the blood can cause hyperosmolality and can increase lactic acidosis.
- Blood sugar levels should be between 60 to 100 mg/dl
- Because main energy provider to the brain is glucose.
- Its demands also increases in Hypoxic ischemic encephalopathy

F) MAINTAIN NORMAL CALCIUM

- In the first two days of life calcium should be given in the maintenance dose of 4ml/kg/day
- Maintenance of calcium levels is essential in newborns with HIE
- It can be given as continuous infusion.

G)MAINTAIN NORMAL HEMATOCRIT

- *In ventilated babies hematocrit should be above 40%*
- .Anemia as well as polycythemia should be identified and treated correctly because polycythemia can result in hyperviscosity with adverse cardiopulmonary complications.

F)TREAT THE SEIZURES

- Initial drug of choice is phenobarbitone dose is 20mg/kg given intravenously and slowly.
- If seizures is not controlled with initial dose give 10mg/kg every 15 minutes.
- It can be given upto 40mg/kg
- Phenytoin can be given if seizures not controlled with maximum dose and ususal initial dose is 20 mg/kg
- Maintainance dose of both drugs are 3-5mg/kg/day given in two divided doses

G)FOLLOW UP

- A complete neurological examination should be done in all newborn with moderate and severe HIE
- Psychometric assessment should be performed in Newborns with HIE around one and half years of age.

H) LONG TERM OUTCOME

- Newborns with moderate and severe HIE needs to be followed up for long periods because they are prone to develop neurological morbidities like seizure ,developmental delay ,cerebral palsy,
- Such newborns require careful evaluation and follow up.
- These babies should be referred to higher centres to provide coordinated comprehensive care.

Hypothermic neuroprotection

- Institute hypothermia if less than 6 hours old according to the following protocol
- For babies who are not being treated with hypothermia because they have a mild encephalopathy, or have moderate / severe encephalopathy but are > 6 hours old, it is essential to avoid hyperthermia

Sepsis

- Take a blood culture and commence antibiotics if there is a possibility of sepsis

Skin integrity

- The sedated or obtunded infant is prone to problems with skin integrity. Change position to reduce pressure sores.

- Make sure infant should not lie on ice packs and that the infant should lie on wet sheets

HYPOTHERMIA

It acts by decreasing the metabolism in grey and white matters in the brain.It also acts by decreasing energy consumption.It reduces the inflammation in the brain by reducing the release of inflammatory mediators like platelet activating factors. It decreases secondary neuronal damage by suppressing free radical activity. Death or severe disability at 18 months of age is reduced by reducing the extent of brain damage

Therapeutic Hypothermia - Cooling [16]

Inclusion Criteria

Infants >36 gestational age who **< 6 hours old** with at least **one** of the following:

- Apgar less than 5 at 10 minutes
- Continued need for resuscitation, including endotracheal or mask ventilation, at 10 minutes after birth
- Documented Acidosis - pH less than 7.00 in umbilical cord or any blood sample (arterial, venous or capillary) within 60 minutes of birth
- Base Deficit ≥ 16 mmol/L in umbilical cord or any blood sample (arterial, venous or capillary) within 60 minutes of birth

Newborns should have 1 or 2 of the below conditions

Moderate to severe encephalopathy, consisting of ALL of*:*

- Consciousness: Altered state of consciousness (reduced or absent response to stimulation)
- Reflexes: Abnormal primitive reflexes (weak or absent suck or Moro response)
- Tone: Abnormal tone (focal or general hypotonia, or flaccid)

OR

- Apparent convulsion or subclinical seizures monitored using Electro encephalogram

PRELIMINARY STEPS BEFORE COOLING

1. Ensure adequate resuscitation and stabilization ,maintain oxygen saturations between 90-95%,maintain blood pressure between 40-50 mmHg and maintain glucose >3.5mmol/L

2. If a decision is made to initiate cooling, then ensure the following:

    - Discuss and advice parents about planned intervention
    - Document the time that cooling is started.
    - Neonate should be kept on an open warmer with the radiant heater.
    - Monitor heart rate,respiratory rate, and continuous saturation monitoring.
    - Measure and document rectal temperature with a digital thermometer inserted 2-3 cm from anal verge every 5-10 minutes
    - Core temperature is likely to above rectal temperature
    - Once the decision to cool has been made ,aim to achieve target temperature zone within 1 hour.

PASSIVE COOLING

It is a process by which neonate allowed to cool because of absence of thermal support.It should be considered while the severity of the neonate clinical encephalopathy is being assessed.

- Neonate should be nursed naked, on an open warmer with radiant heater turned off and the nappy should in position.
- If a head box oxygen is required, do not humidity:If the baby is on ventilator use standard humidifier settings.
- Timing of commencing hypothermia should be recorded and document temperature every 15 minutes.
- If the neonate temperature reaches 33.5^0 C use warm blankets or use radiant warmer on manual control to maintain temperature in the target range of $33\text{-}34^0$ C

ACTIVE COOLING

It is usually done to start hypothermia or increase the hypothermic effects.It utilizes cold packs .Frozen packs should not be used.

ORGAN DYSFUNCTION IN PERINATAL ASPHYXIA[20]

CNS	Hypoxic ischemic encephalopathy, intracranial hemorrhage, seizures, long-term neurological sequlae

Cardiac	Myocardial dysfunction, valvular dysfunction, rhythm abnormalities, congestive cardiac failure
Renal	Hematuria, acute tubular necrosis, renal vein thrombosis
Pulmonary	Delayed adaptation, respiratory failure, meconium aspiration, surfactant depletion, primary pulmonary hypertension
GI tract	Necrotizing enterocolitis, hepatic dysfunction
Hematological	Thrombocytopenia, coagulation abnormalities
Metabolic	Acidosis, hypoglycemia, hypocalcemia, hyponatremia

COMPLICATIONS

- In the heart, severe or prolonged asphyxia result in hypoxic cardiomyopathy that can present with poor myocardial contractility and heart failure.[2]
- In the kidneys, reduced blood flow results in cortical necrosis or acute tubular necrosis with features of hematuria, proteinuria and oliguria.
- In the GIT, hypoxia predisposes to poor intestinal motility and ileus which leads to perforation, ulceration with hemorrhagic necrosis.
- In the hematopoietic system, asphyxia depresses bone marrow and initiates intravascular coagulopathy ,which leads to thrombocytopenia,

prolonged prothrombin time and partial thromboplastin time with evidence of bleeding.

PROGNOSIS

In asphyxiated newborn predicting the neurodevelopmental outcome is extremely difficult.

- Explanations for the lack of predictive success include functional and anatomic plasticity, interindividual variability for the same insult, differences in provision of services, and differences in socioeconomic status .
- Outcome mainly based on the degree of the injury and the extent of brain damage.
- There is a threshold of injury beyond which the brain is damaged. Various factors can influence the final outcome which include placental-fetal blood flow, energy reserves, or presence of cerebral anomalies.
- It is often difficult to determine the duration of the insult because the vast majority of insults occurs in utero and because adequate fetal surveillance is difficult.

- Certain clinical factors as well as the results of brain imaging studies can help identify infants with a poor prognosis .

PREDICTORS OF NEUROLOGICAL MORBIDITY AND MORTALITY AFTER PERINATAL HYPOXIC ISCHAEMIC INSULT[20]

- Extended very low APGAR scores (at 20 minutes)
- Time to establish spontaneous respiration (for 30 or more minutes)
- Neonatal neurological examination(severe HIE)
- Brain imaging (USG, MRI)
- Other investigations (EEG, amplitude integrated EEG, Evoked potentials like BERA)

DEVELOPMENTAL ASSESSMENT CAN BE DONE IN SEVERAL WAYS

1)Birth to two years:

TRIVANDRUM DEVELOPMENTAL SCREENIG CHART:

It is a simple screening tool to assess development in large populations below two years of age and it is used by the anganwadi workers .The left end of the horizontal dark line indicates age at which 3% of the children passed the item. The right end represents age at which 97% of children passed the item. If the child chronological age fall to left side of the line it is considered to be developmental delay.

2)Two to four years:

DEVELOPMENTAL ASSESSMENT TOOL FOR ANGANWADI

Another one is DENEVER DEVELOPMENT SCREENING TESTII

It is quick and simple screening tool for developmental assessment .It comprises of 125 items divided into four categories.1)gross motor2)fine motor3)language4)personal and social skills. The child age drawn as a vertical line on the chart and examiners administer the items bisected by the lines. Performance of the child rated as pass, caution and delay.

The Vineland Social Maturity Scale measures social competence, self-help skills and adaptive behavior from infancy to adulthood. The Vineland scale consists of a 117-item interview with a parent or other primary caregiver

William T.Mahle et all stated that Bayley scale of infant development has sensitivity of 68% and specificity of 80%

Weschler intelligence scale for children-Indian adaptation.

It uses verbal and nonverbal performance scales used to assess verbal and non verbal intelligence. Score of the scale ranges from 0 to 20

Development activities inventory(DASI)II

Developmental assessment: Developmental assessment should be done according to the corrected age.

Assessment of milestones must be in four domains - gross motor, fine motor, language, and personal. Corrected age should be mentioned while performing developmental assessment. Based on the date of achievement of milestones in a particular domain and the expected age of achieving them, the developmental age can be calculated. The infants found to be delayed in any domains must undergo developmental assessment by using DASII. It should de performed by a clinical psychologist.. Motor scale assesses control of gross and fine motor muscle groups. Mental scale assesses cognitive, personal and social skills development. DASII can assess both mental development index and psychomotor development index. The age placement of the item at the total score rank of the scale is noted as the child developmental age. This converts the child total scores to his motor age (MoA) and mental age(MeA). The respective ages are used to calculate his motor and mental

development quotients respectively by comparing them with his chronological age and multiplying it by 100. (DMoQ = MoA/CA x 100 and DMeQ = MeA/CA x 100).

The composite DQ is derived as an average of DMoQ and DMeQ. It is designed for early detection of development delay with special focus on young children with language impairment whose cognitive abilities may not be accurately screened with a tool that requires the child to follow spoken instructions. DASI-II instructions may be either verbal or visual. There are 67 items which can be administered in one or two settings. Reliability and validity studies found correlation coefficient ranging from 0 .87 to 0.95.

Description of scales

DASII scale is a point scale with items arranged in ascending order or age placement for both motor and mental scales. The items in the two scales are classified into content clusters under different areas of development. There are five clusters of motor items and 10 clusters of mental items.

Motor clusters

I. Neck control

II. Body control

III. Locomotion I (Coordinated movements)

IV. Locomotion II (Skills)

V. Manipulation

Mental clusters

I. Cognizance (Visual)

II. Cognizance (Auditory)

III. Reaching, manipulation and exploring

IV. Memory

V. Social interaction and imitative behavior

VI. Language I (Vocabulary and comprehension)

VII. Understanding of relationship

VIII. Differentiation by use, shapes and movements

IX. Manual dexterity

The content clusters have great utility in clinical practice. They may be used in analyzing the child's performance in each area of development obtaining a profile of development with indication of areas of delay in development.

It helps to plan intervention strategy with reference to child's strengths and weaknesses. It aids in effective counseling of parents for home based stimulation program.

Differential diagnosis with DASII

It is possible not only to identify delays and areas of delays with DASII but cluster analysis can also help in differential diagnosis.

A Down's syndrome baby will have better motor than mental profile .A high functioning autistic child will have almost normal motor profile and relatively low mental but, especially low on language, social interaction. He is likely to do better on memory, understanding of relationships or form boards.

- A cerebral palsy child will score low on motor items, imitative, skills but better on language development, especially receptive language.He may do poorly on timed items, like manipulation and manual dexterity clusters.

- A child with low stimulational and early deprivation may show adequate score on motobut lower on mental clusters.

- Thus, in trained hands, the DASII is a very comprehensive and effective tool often considered the gold standard for developmental assessment.

- It should be an integral part of any developmental clinic where effective intervention is planned.

Points to Remember

- Developmental assessment should be an integral part of NICU (Neonatal intensive care unit)
- Developmental screening be done in all high risk infant as early as 3-6 months of age
- DASII (Developmental assessment scales for Indian infants) is a very effective comprehensive and useful tool which is standardized in Indian babies

JUSTIFICATION OF STUDY

Simple non invasive clinical tool to select ideal candidate for neuro protective therapy, to do early intervention like physiotherapy, developmental assessment,

occupational therapy, to minimize disability in future, to counsel the parents regarding prognosis early.

AIM :To determine the ability of THOMPSON SCORE in newborn infant with HIE at birth in predicting neurodevelopmental outcome at 9 months of age.

STUDY POPULATION: Child born with signs of HIE at birth are my study population.50 in each arm as exposed and unexposed group(including 10% lost to follow up)

Exposed-Thompson score more than 10

Unexposed-Thompson score equal or less than 10

Study period-September 2014 to August 2015

Methodology-Term infants of 37 weeks of gestation or more (as determined by the Ballard score) are selected for the study with clinical signs of HIE developed after birth.

Cranial ultrasound is the objective investigation available.Atleast one cranial ultrasound was carried out,usually prior to hospital discharge.100 neonates who met the inclusion criteria were recruited in to study.Of the 100 neonates 8 neonates died during neonatal period .Of the 92 who survived,5 neonates lost to followup.

An detailed developmental assessment was conducted at 9 months of age by DASII .Outcome was considered abnormal if there is developmental delay ,defined

by composite developmental quotient .If it less than 70 it is severe delay and if it is between 70-85 it is moderate delay.

T his prospective cohort study was conducted at the RSRM Hospital NICU and the Follow up clinic.

INCLUSION CRITERIA-

1)Full term babies with Apgar score(i.e five minute Apgar score of less than or equal to 7

2) Sick infants with symptoms and signs of HIE (respiratory arrest, apnea, posturing, movement disorder, impaired sucking, swallowing and feeding)

EXCLUSION CRITERIA:

1) Infants> 6hrs of age

2) Major congenital abnormality or syndromes that include brain dysgenesis

3) Preterm babies.

4)Intraventricular hemorrhage.

5)Neonatal sepsis.

Infants scored by THOMPSON SCORE within 6 hrs of birth and for 7 consecutive days. Infants followed up at 9 months of age. One cranial ultrasound should be done

prior to discharge. Detailed neurological and development assessment should be done.

Table 1. Hypoxic ischaemic encephalopathy score.

Sign	Score 0	1	2	3
Tone	Normal	Hyper	Hypo	Flaccid
LOC	Normal	Hyper alert, stare	Lethargic	Comatose
Fits	None	Infreq $< 3\ d^{-1}$	Frequent>2/day	
Posture	Normal	Fisting, cycling	Strong, distal flexion	Decerebrate
Moro	Normal	Partial	Absent	
Grasp	Normal	Poor	Absent	
Suck	Normal	Poor	Absent ± bites	
Resp.	Normal	Hypervent	Brief apnoea	IPPV (apnoea)
Font'l	Normal	Full, not tense	Tense	
				Total score per day-

It is a clinical tool comprising of a set of clinical signs associated with CNS dysfunction. It is used to assess status of a child following birth asphyxia.

In scoring system, a score of 0 is normal and maximum score is 22 which signifies worst possible status of HIE. Infants scoring 1-10 are considered to have mild HIE,11-14 have moderate HIE,15-22 are considered to have severe HIE. This is modified sarnat scoring system. Infant neurological assessment should be conducted using DASI II by paediatrician.

SAMPLING TECHNIQUE

Consequetive sampling technique was used to collect cases and controls in each arm. Epi info 7 was used for data analysis .Incidence of abnormal neurological outcome will be estimated along with 95% confidence interval .Identifying influencial factors for bad neurological outcome.

Correlation and regression analysis will be done for Thompson score and DASII developmental quotient.

RESULTS:

100 neonates who met the inclusion criteria were recruited in to study. Of the 100 neonates 8 neonates died during neonatal period .Of the 92 who survived,5 neonates lost to followup reasons for which are not known. For understanding purpose let us assume exposed as cases and unexposed as controls.

COMPARISON OF SEX DISTRIBUTION AMONG CASES AND CONTROLS

SEX * GROUP

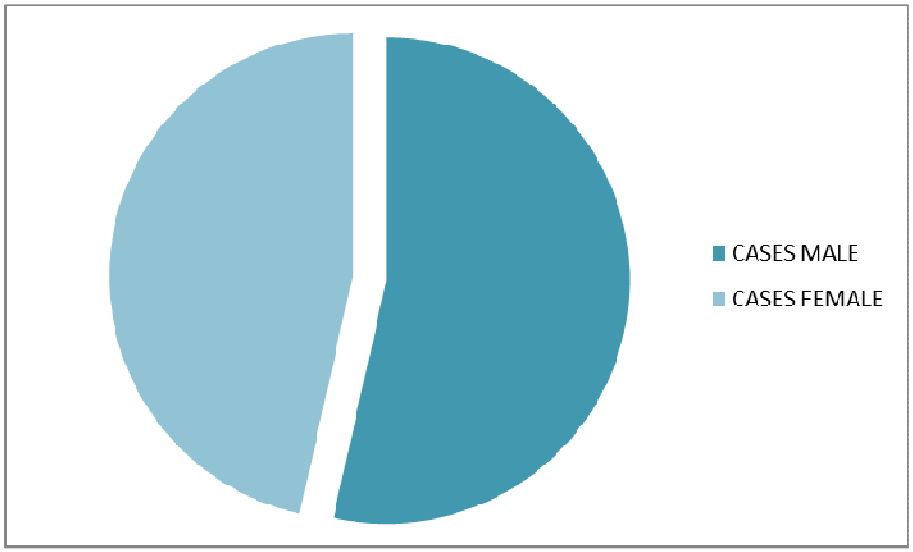
Crosstab

			GROUP		
			CASE	CONTROL	Total
SEX	MALE	Count	23	19	42
		% within GROUP	53.5%	44.2%	48.8%
	FEMALE	Count	20	24	44
		% within GROUP	46.5%	55.8%	51.2%
Total		Count	43	43	86
		% within GROUP	100.0%	100.0%	100.0%

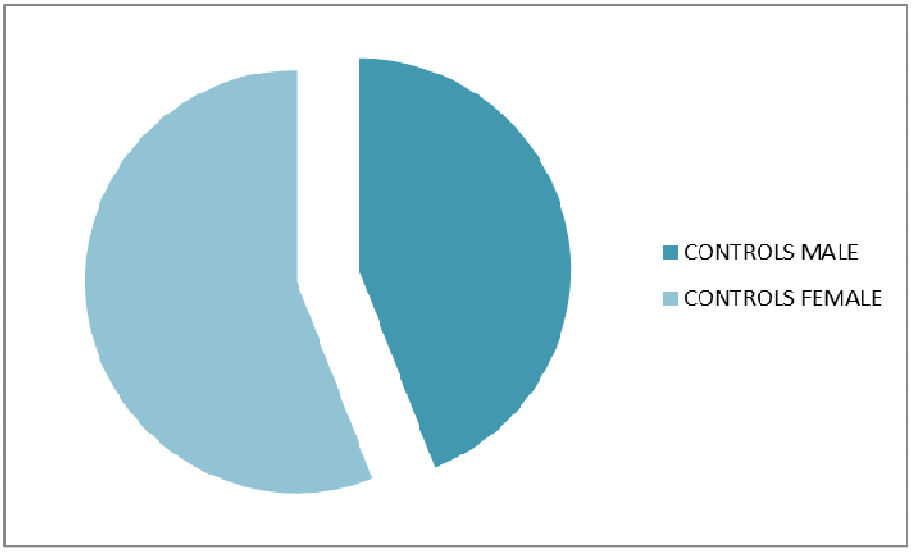
DESCRIPTION OF BABIES WITH HIE

Among 43 babies in case group 23(53.5%) infants belongs to male sex and 20 (46.5%) belong to female sex. Among 43 babies in control group 19 (44.2%) belong to male and 24(55.8%) belong to female sex.

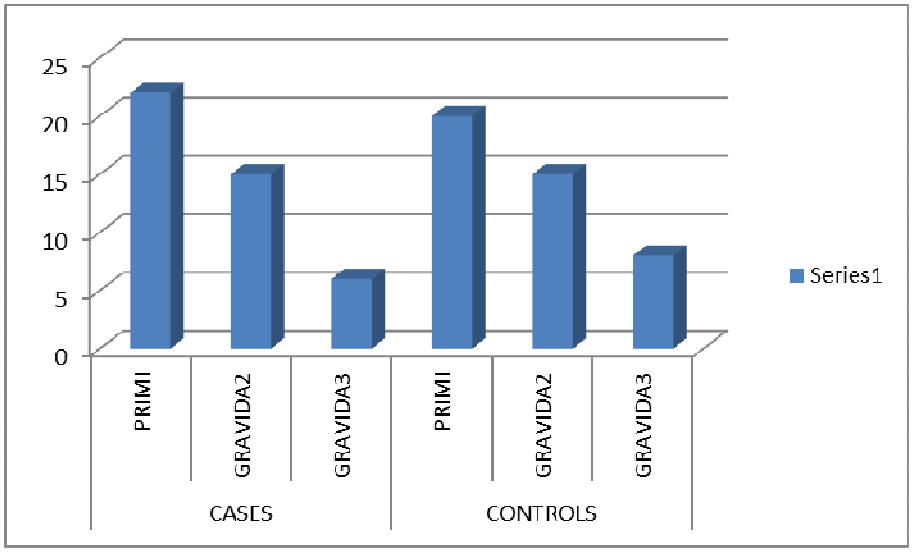
SEX DISTRIBUTION AMONG CASES



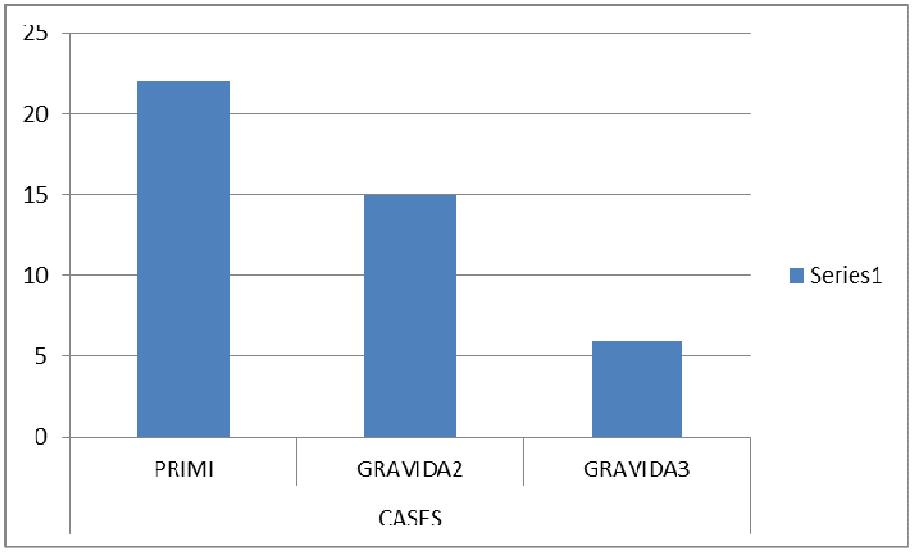
SEX DISTRIBUTION AMONG CONTROLS



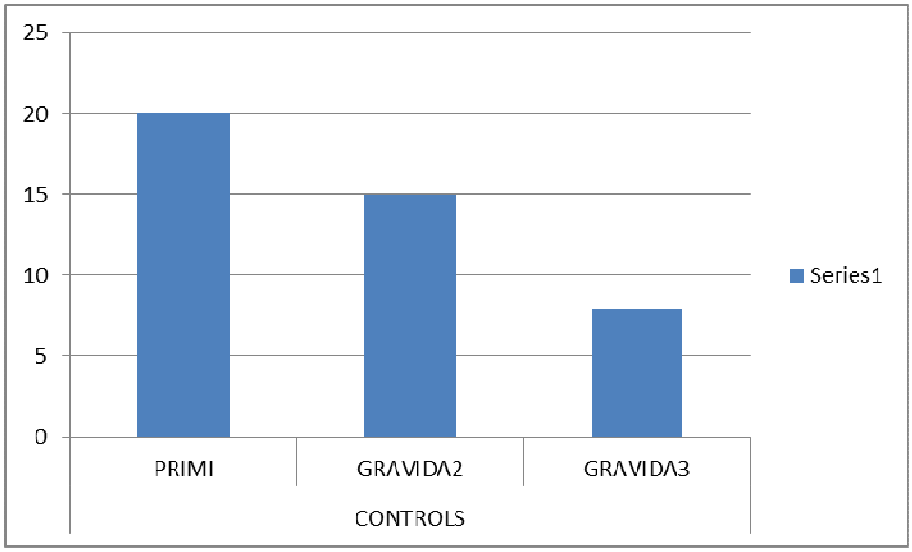
PARITY DISTRIBUTION IN CASES AND CONTROLS



PARITY DISTRIBUTION AMONG CASES GROUP



PARITY DISTRIBUTION AMONG THE CONTROL GROUP



Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.745[b]	1	.388		
Continuity Correction[a]	.419	1	.518		
Likelihood Ratio	.746	1	.388		
Fisher's Exact Test				.518	.259
Linear-by-Linear Association	.736	1	.391		
N of Valid Cases	86				

a. Computed only for a 2x2 table

b. 0 cells (.0%) have expected count less than 5. The minimum expected count is 21. 00.

COMPARISON OF PARITY AMONG CASE AND CONTROL GROUP

Crosstab

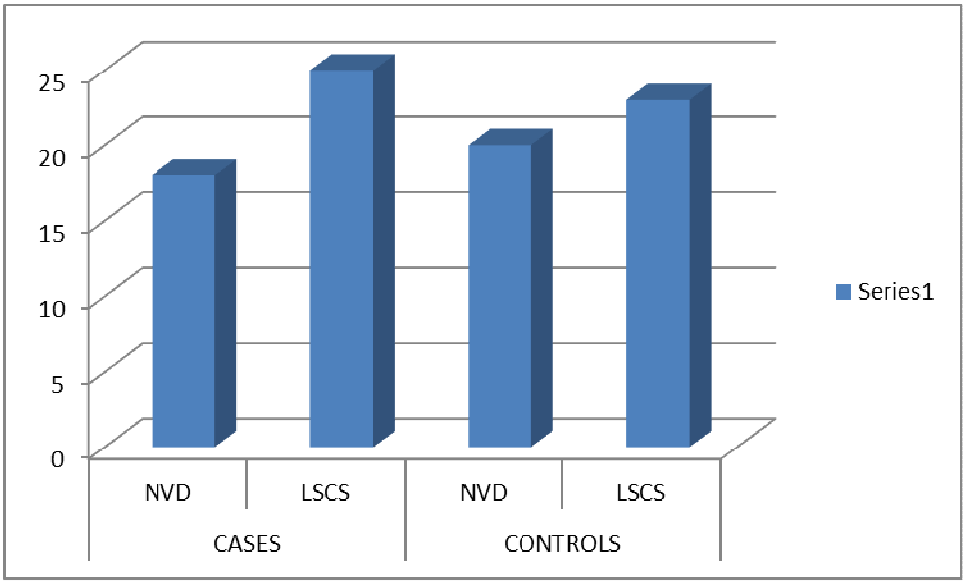
			GROUP		
			CASE	CONTROL	Total
PARITY	PRIMI	Count	22	20	42
		% within GROUP	51.2%	46.5%	48.8%
	GRAVIDA 2	Count	15	15	30
		% within GROUP	34.9%	34.9%	34.9%
	GRAVIDA 3	Count	6	8	14
		% within GROUP	14.0%	18.6%	16.3%
Total		Count	43	43	86
		% within GROUP	100.0%	100.0%	100.0%

Chi-Square Tests

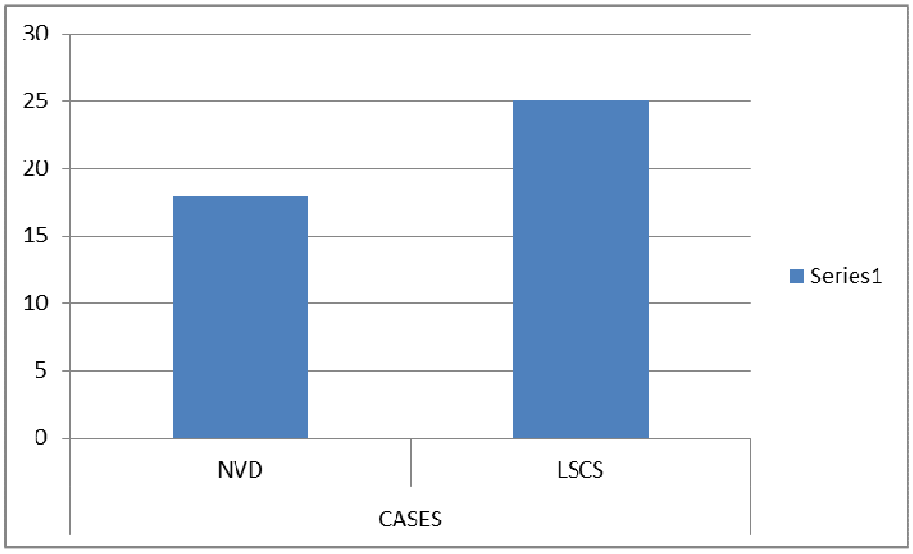
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.381[a]	2	.827
Likelihood Ratio	.382	2	.826
Linear-by-Linear Association	.337	1	.561
N of Valid Cases	86		

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 7.00.

MODE OF DELIVERY * GROUP



MODE OF DELIVERY AMONG CASES GROUP

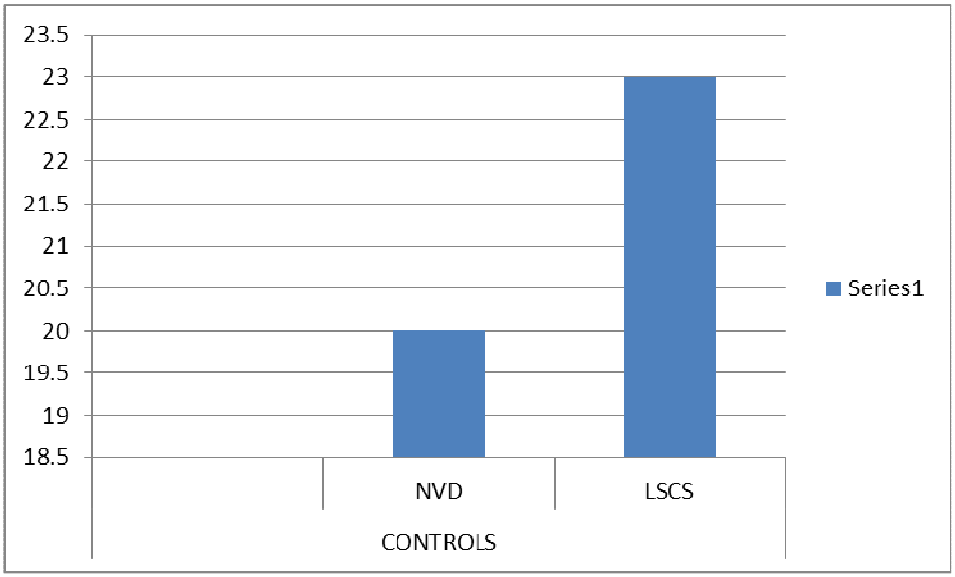


PARITY AND MODE OF DELIVERY AMONG HIE BABIES

- Among cases 18(41.9%) babies born by Normal vaginal delivery and 25(58.1%) born by LSCS.Among 43 controls 20(46.5%) born by Normal vaginal delivery and 23(53.5%) born by LSCS.

- Among 43 cases, 22 babies born to primi mothers and 15 babies born to second gravida mothers and 6 babies born to third gravida mothers.Among controls ,20 babies born to primi mothers ,15 babies born to second gravida mothers and 8 babies born to third gravida mothers.

MODE OF DELIVERY AMONG CONTROL GROUP



COMPARISM OF MODE OF DELIVERY AMONG CASES AND CONTROL GROUP

Crosstab

			GROUP		
			CASE	CONTROL	Total
MODE OF DELIVER	NVD	Count	18	20	38
		% within GROUP	41.9%	46.5%	44.2%
	LSCS	Count	25	23	48
		% within GROUP	58.1%	53.5%	55.8%
Total		Count	43	43	86
		% within GROUP	100.0%	100.0%	100.0%

Chi-Square Tests

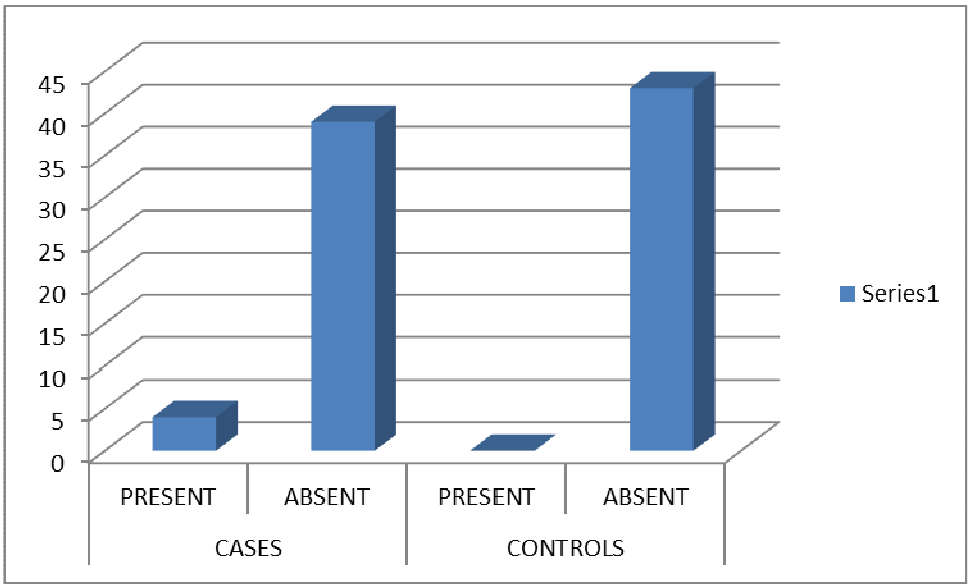
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.189[b]	1	.664		
Continuity Correction[a]	.047	1	.828		
Likelihood Ratio	.189	1	.664		
Fisher's Exact Test				.828	.414
Linear-by-Linear Association	.186	1	.666		
N of Valid Cases	86				

a. Computed only for a 2x2 table

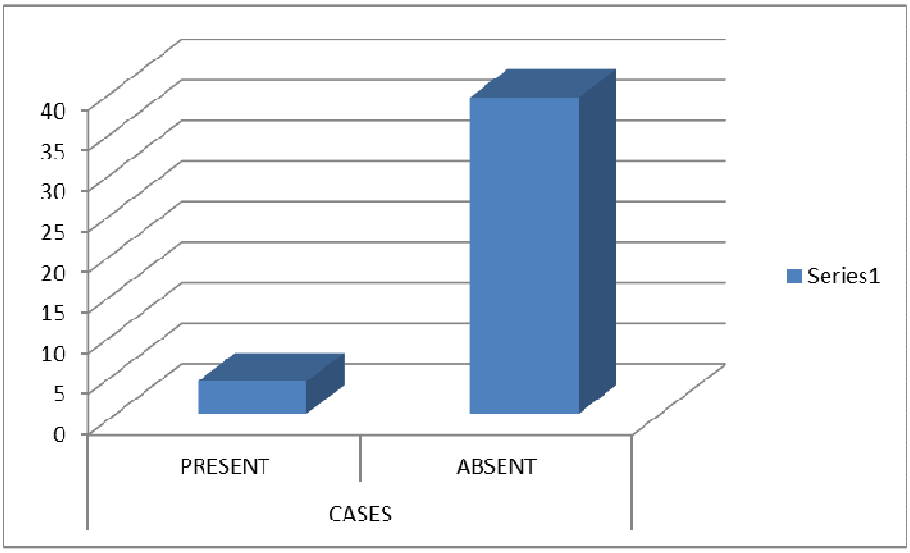
b. 0 cells (.0%) have expected count less than 5. The minimum expected count is 00.

CONVULSIONS * GROUP

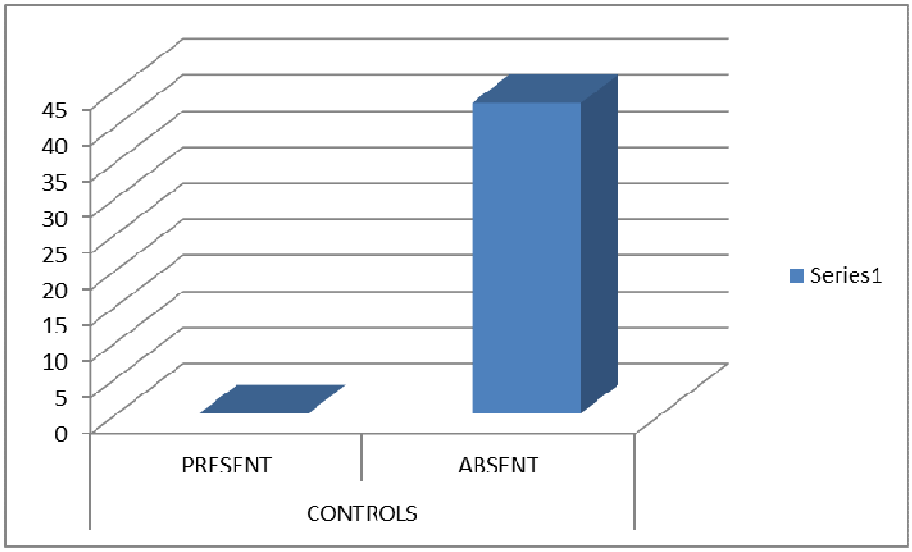
COMPARISM OF CONVULSION AMONG CASES AND CONTROL GROUP



CONVULSIONS AMONG CASES



CONVULSIONS AMONG CONTROLS



CONVULSIONS AMONG CASES AND CONTROLS

Among cases 4 developed convulsions i.e 9.3% of cases.Rest 39 cases (90.7%) did not develop convulsions.Among 43 controls none of babies had seizures.

COMPARISM OF CONVULSIONS AMONG CASES AND CONTROLS

	GROUP		TOTAL
	CASES	**CONTROLS**	
CONVULSIONS YES COUNT%WITHIN	4(9.3%)	0(0%)	4(4.7%)
NO COUNT%WITHIN	39(90.7%)	43(100%)	82(95.3%)
TOTAL	**43**(100%)	**43(100%)**	**86**

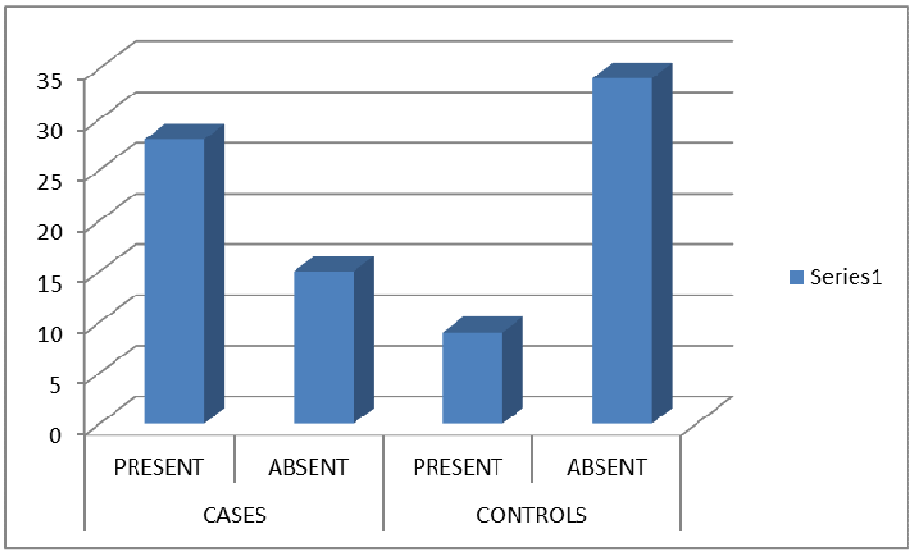
Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Squa	4.195[b]	1	.041		
Continuity Correct[a]	2.360	1	.125		
Likelihood Ratio	5.740	1	.017		
Fisher's Exact Tes				.116	.058
Linear-by-Linear Association	4.146	1	.042		
N of Valid Cases	86				

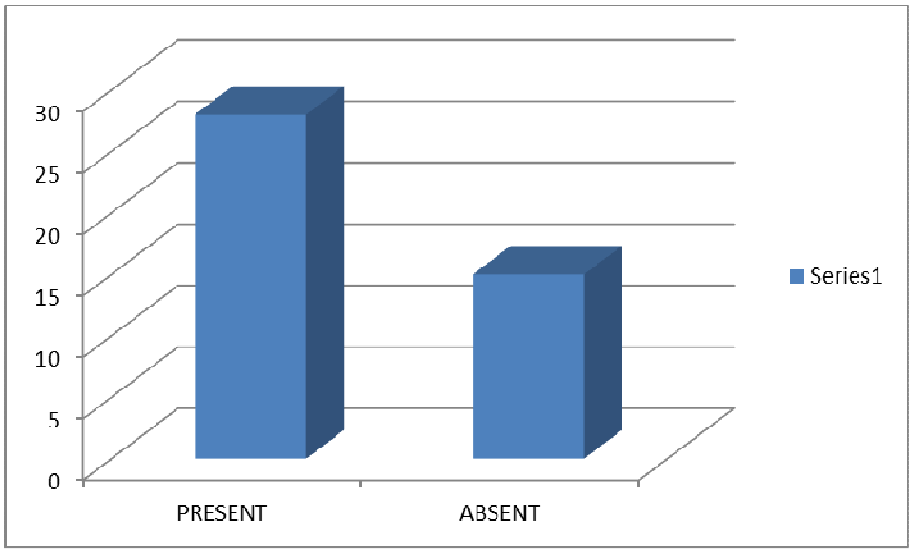
a. Computed only for a 2x2 table

b. 2 cells (50.0%) have expected count less than 5. The minimum expe
00.

COMPARISM OF DEVELOPMENTAL DELAY AMOND CASES AND CONTROLS



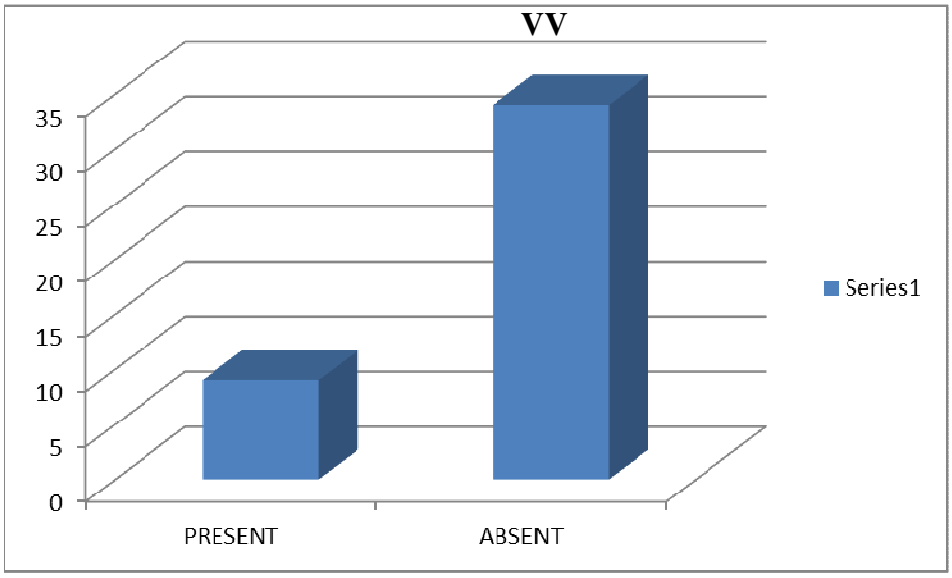
DEVELOPMENTAL DELAY AMONG CASES



DEVELOPMENTAL DELAY AND DEVELOPMENTAL QUOTIENT

Among cases mean developmental quotient was 71.42 and among the controls it was 85.77.Among cases 28(65.1%) had developmental delay, and 15(34.9%) has normal development .Among the 43 controls 9 (20.9%) has developmental delay and 34(79.1%) has normal development

DEVELOPMENTAL DELAY AMONG CONTROL GROUP



Crosstab

			GROUP		
			CASE	CONTROL	Total
DEVELOPMENTAL DELAY	PRESENT	Count	28	9	37
		% within GROUP	65.1%	20.9%	43.0%
	ABSENT	Count	15	34	49
		% within GROUP	34.9%	79.1%	57.0%
Total		Count	43	43	86
		% within GROUP	100.0%	100.0%	100.0%

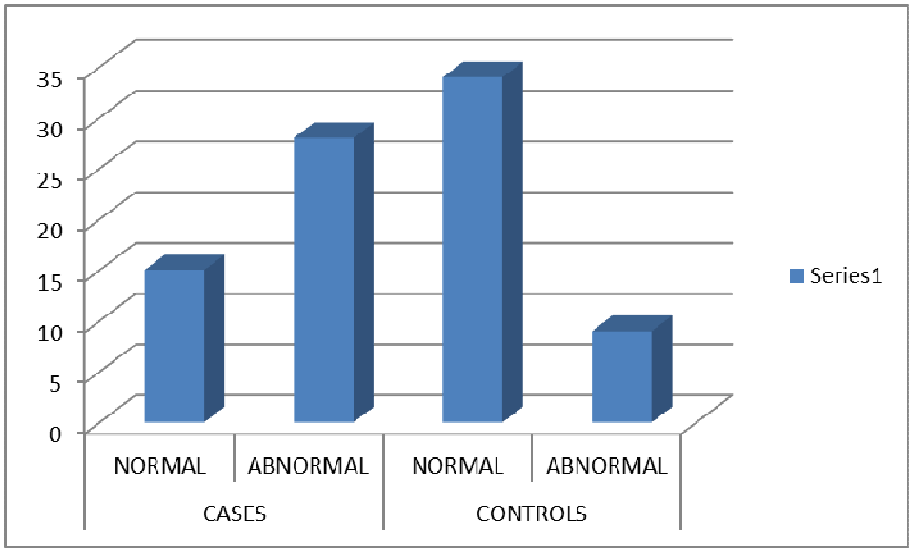
Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	17.124[b]	1	.000		
Continuity Correction[a]	15.369	1	.000		
Likelihood Ratio	17.803	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	16.925	1	.000		
N of Valid Cases	86				

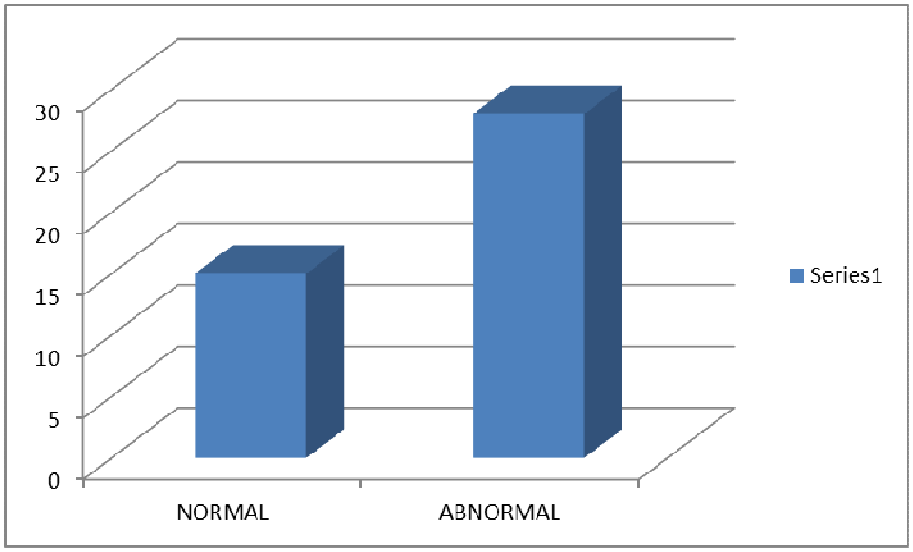
a. Computed only for a 2x2 table

b. 0 cells (.0%) have expected count less than 5. The minimum expected count is 18. 50.

COMPARISM OF OUTCOME BETWEEN CASES AND CONTROL GROUP



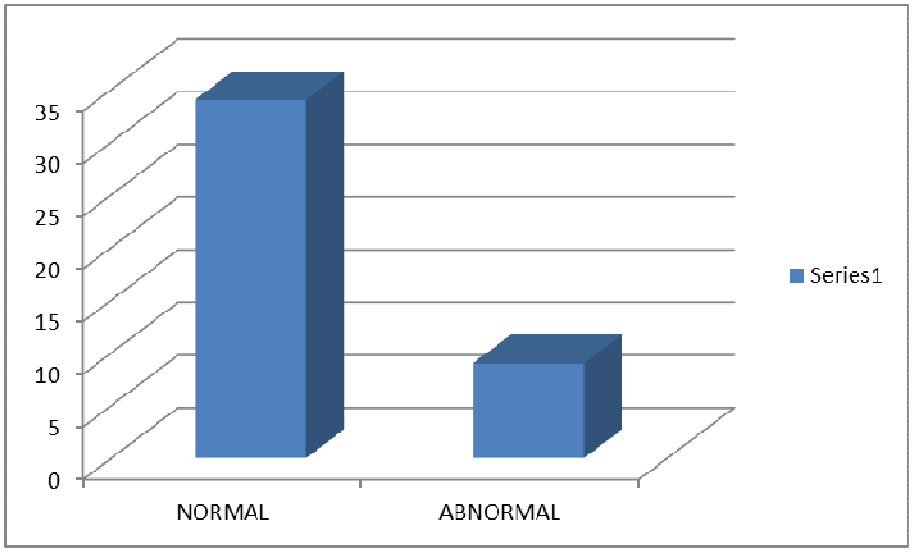
OVERALL OUTCOME AMONG CASES



OVERALL OUTCOME AMONG CASES AND CONTROLS

Among 43 cases 28 babies i.e 65.1% of babies had overall abnormal outcome.Among 43 controls 9 babies i.e 20.9% of babies had overall abnormal outcome.

OVERALL OUTCOME AMONG CONTROLS



Crosstab

			GROUP		
			CASE	CONTROL	Total
OVERALL OUTCOM	NORMAL	Count	15	34	49
		% within GROU	34.9%	79.1%	57.0%
	ABNORMAL	Count	28	9	37
		% within GROU	65.1%	20.9%	43.0%
Total		Count	43	43	86
		% within GROU	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	17.124[b]	1	.000		
Continuity Correction[a]	15.369	1	.000		
Likelihood Ratio	17.803	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	16.925	1	.000		
N of Valid Cases	86				

a. Computed only for a 2x2 table

b. 0 cells (.0%) have expected count less than 5. The minimum expected count is 18.50.

COMPARISON OF BIRTH WEIGHT BETWEEN CASES AND CONTROL GROUP

T-Test

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
BIRTH WEIGHT	CASE	43	2.944	.4114	.0627
	CONTROL	43	2.883	.3442	.0525
GESTATIONAL AGE	CASE	43	38.14	.804	.123
	CONTROL	43	38.02	.831	.127

T-Test

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
BIRTH WEIGHT	Equal variances assumed	1.443	.233	.742	84	.460	.0607	.0818	-.1020	.2234
	Equal variances not assumed			.742	81.462	.460	.0607	.0818	-.1020	.2234
GESTATIONAL A(	Equal variances assumed	.000	.991	.660	84	.511	.116	.176	-.234	.467
	Equal variances not assumed			.660	83.912	.511	.116	.176	-.234	.467

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
APGAR SCORE1MIN	CASE	43	2.23	.996	.152
	CONTROL	43	3.70	1.505	.229
APGAR SCORE5MIN	CASE	43	5.07	1.261	.192
	CONTROL	43	6.00	1.069	.163

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
APGAR SCORE1M	Equal variances assumed	10.668	.002	-5.324	84	.000	-1.465	.275	-2.012	-.918
	Equal variances not assumed			-5.324	72.887	.000	-1.465	.275	-2.014	-.917
APGAR SCORE5M	Equal variances assumed	.778	.380	-3.690	84	.000	-.930	.252	-1.432	-.429
	Equal variances not assumed			-3.690	81.808	.000	-.930	.252	-1.432	-.429

Mann-Whitney Test

Ranks

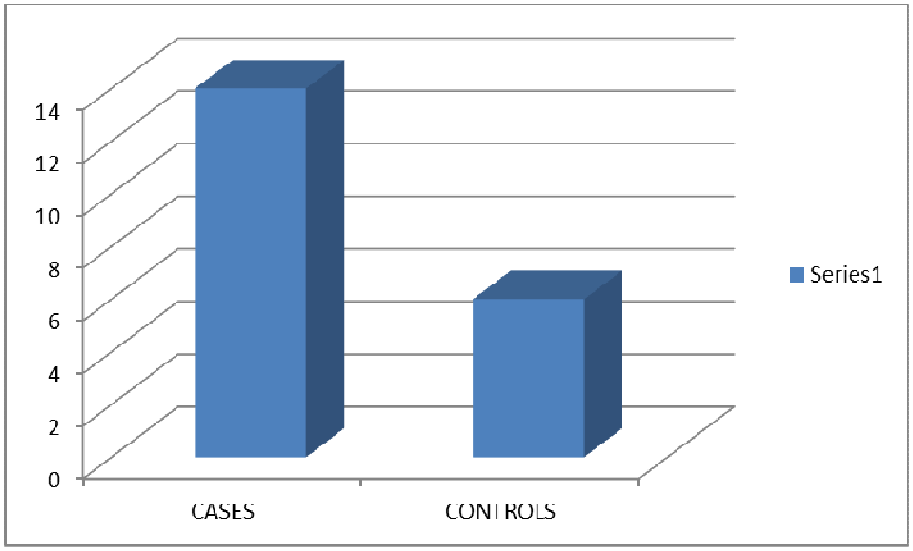
	GROUP	N	Mean Rank	Sum of Ranks
APGAR SCORE1MIN	CASE	43	31.52	1355.50
	CONTROL	43	55.48	2385.50
	Total	86		
APGAR SCORE5MIN	CASE	43	34.51	1484.00
	CONTROL	43	52.49	2257.00
	Total	86		

Test Statistics[a]

	APGAR SCORE1MIN	APGAR SCORE5MIN
Mann-Whitney U	409.500	538.000
Wilcoxon W	1355.500	1484.000
Z	-4.552	-3.445
Asymp. Sig. (2-tailed)	.000	.001

a. Grouping Variable: GROUP

COMPARISM OF THOMPSON SCORE BETWEEN CASE AND CONTROL GROUP



THOMPSON SCORE AMONG CASES AND CONTROLS

Among 43 cases mean Thompson score was 14.42 and among 43 controls mean Thompson score was 6.47.

T-Test

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
THOMPSON SCORE	CASE	43	14.42	3.547	.541
	CONTROL	43	6.47	1.932	.295

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
THOMPSON SCO	Equal variances assumed	7.707	.007	12.913	84	.000	7.953	.616	6.729	9.178
	Equal variances not assumed			12.913	64.894	.000	7.953	.616	6.723	9.184

NPar Tests

Mann-Whitney Test

Ranks

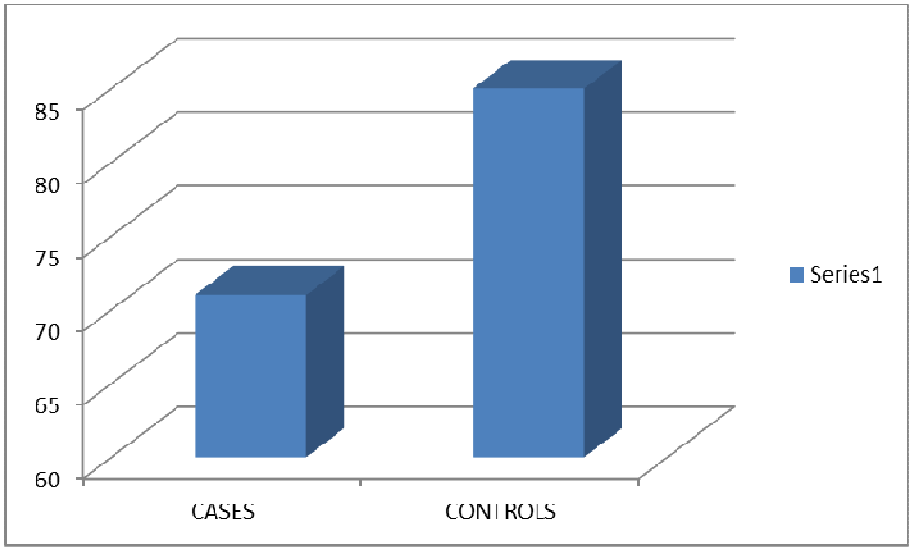
	GROUP	N	Mean Rank	Sum of Ranks
THOMPSON SCORE	CASE	43	64.00	2752.00
	CONTROL	43	23.00	989.00
	Total	86		

Test Statistics[a]

	THOMPSON SCORE
Mann-Whitney U	43.000
Wilcoxon W	989.000
Z	-7.633
Asymp. Sig. (2-tailed)	.000

a. Grouping Variable: GROUP

COMPARISON OF DEVELOPMENTAL QUOTIENT AMONG CASES AND CONTROLS



DEVELOPMENTAL DELAY AND DEVELOPMENTAL QUOTIENT

Among cases mean developmental quotient was 71.42 and among the controls it was 85.77.Among cases 28(65.1%) had developmental delay, and 15(34.9%) has normal development .Among the 43 controls 9 (20.9%) has developmental delay and 34(79.1%) has normal development

T-Test

Group Statistics

	GROUP	N	Mean	Std. Deviation	Std. Error Mean
DEVELOPMENT QUOTIENT	CASE	43	71.42	21.818	3.327
	CONTROL	43	85.77	14.851	2.265

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
DEVELOPMENT QUOTIENT	Equal variances assumed	10.346	.002	-3.565	84	.001	-14.349	4.025	-22.353	-6.345
	Equal variances not assumed			-3.565	74.043	.001	-14.349	4.025	-22.368	-6.329

DISCUSSION

Hypoxic ischaemic encephalopathy is associated with significant morbidity and mortality in full term infant. This study aimed as assessing role of Thompson score in predicting neurodevelopmental outcome in term babies who suffered birth asphyxia.

100 neonates who met the inclusion criteria were recruited in to study.Of the 100 neonates 8 neonates died during neonatal period .Of the 92 who survived,5 neonates lost to followup.

In this study ,it was found that HIE score was highly specific in detecting morbidity among neonates who had moderate and severe HIE.The study also revealed developmental delay was more with increasing HIE score.Others studies have shown a similar finding that severely asphyxiated infants have a high mortality within first 72 hours of life

Among 43 babies in case group 23(53.5%) infants belongs to male sex and 20 (46.5%) belong to female sex.Among 43 babies in control group 19 (44.2%) belong to male and 24(55.8%) belong to female sex.

Among cases mean birth weight is 2.944 and mean birth weight among controls mean birth weight is 2.883.Mean gestational age among cases was 38 weeks and among the controls also it was same.In this study, among the cases 18(41.9%) babies born by Normal vaginal delivery and 25(58.1%) born by LSCS. Among 43 controls 20(46.5%) born by Normal vaginal delivery and 23(53.5%) born

by LSCS. Among 43 cases, 22 babies born to primi mothers and 15 babies born to second gravida mothers and 6 babies born to third gravida mothers. Among controls ,20 babies born to primi mothers ,15 babies born to second gravida mothers and 8 babies born to third gravida mothers. This study also revealed that among 43 cases mean Thompson score was 14.42 and among 43 controls mean Thompson score was 6.47.

In this study it was found that 4 cases developed convulsions i.e 9.3% of cases. Rest 39 cases (90.7%) did not develop convulsions. Among 43 controls none of babies had seizures. This study also revealed that mean developmental quotient among cases was 71.42 and among the controls it was 85.77.Among cases 28(65.1%) had developmental delay, and 15(34.9%) has normal development .Among the 43 controls 9 (20.9%) has developmental delay and 34(79.1%) has normal development. This study also revealed among 43 cases 28 babies i.e 65.1% of babies had overall abnormal outcome .Among 43 controls 9 babies i.e 20.9% of babies had overall abnormal outcome.

From the previous studies it was known that positive predictive values for poor outcome in moderate and severe HIE is 90% and 100% respectively and negative predictive value for the scoring system was 81.4% sekala D et al.

C Thompson et all stated that sensitivity and specificity of Thompson score in predicting neurodevelopmental outcome for maximum score and abnormal on day 7 is 100% and 93% respectively.

Alom R Horn et all stated sensitivity for abnormal outcome is 100% and 61% specificity. He Stated that Thompson score has sensitivity 90% and specificity of 92% in predicting moderate to severe encephalopathy as compared to aEEG .Positive predictive value and negative predictive value of HIE score in predicting neurodevelopmental outcome were 89% and 82% respectively in our study. Our results are concominant with C Thompson et all who found that positive predictive value of maximum score is 92 % and negative predictive value of 82% for abnormal outcome with sensitivity and specificity of 71% and 96% respectively.

CONCLUSIONS:

- The HIE scoring system used in this study is highly predictive of neonatal outcome in terms of early morbidity.

- Neurological assessment done at 9 months of age using DASII observed developmental delay by estimating developmental quotient and observing Neurological abnormalities in the form of seizures.. Neurological morbidities are correlating to Thompson score.

RECOMMENDATIONS

- It should be performed in all newborns with HIE so that the clinician can identify the infants who are at high risk of developing abnormal neurodevelopmental outcome.

- It is easy tool for the clinicians to counsel the parents about abnormal neurodevelopmental outcome of their babies in earlier periods of life.

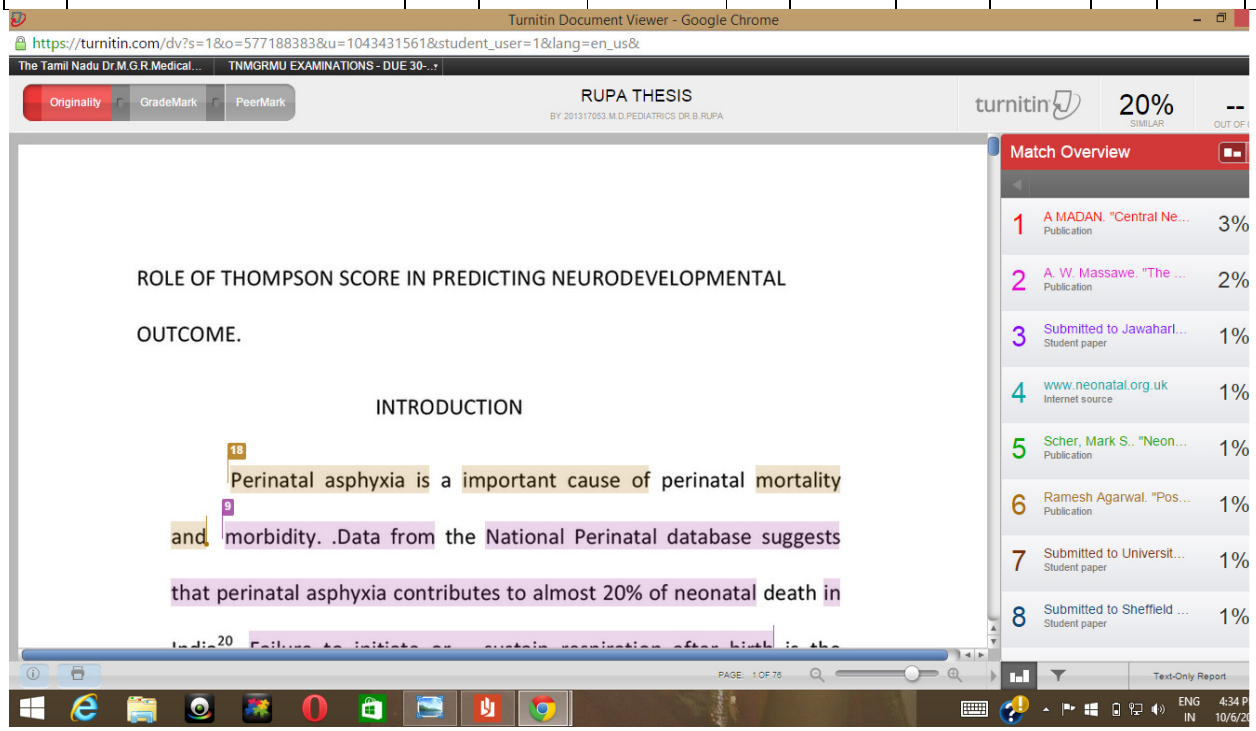
	NAME	SEX	BIRTH WEIGHT	GESTATIONAL AGE	PARITY	MODE OF DELIVERY	APGAR SCORE		THOMPSON SCORE	CONVULSIONS	DEVEL QUOTI
				(weeks)			1 MIN	5MIN			
1	B/O SARANYA	M	2.6KG	37	1	NVD	2	3	15	YES	
2	B/O VENKATARAMA	F	3.25KG	38	3	NVD	3	5	16	NO	
3	B/O KUMARI	F	2.54KG	37	2	LSCS	2	4	18	YES	
4	B/O DIVYA	F	3.25KG	39	1	LSCS	2	5	14	NO	
5	B/O MAHADEVI	M	2.75KG	39	2	LSCS	2	5	13	NO	
6	B/O NANDHINI	F	2.5KG	37	1	LSCS	1	5	13	NO	
7	B/O SUGANYA	M	3.3KG	38	1	LSCS	2	6	17	YES	
8	B/O MANJULA	F	3.2KG	39	1	LSCS	2	5	16	NO	
9	B/O SUMITRA	M	2.56KG	39	1	LSCS	1	6	17	NO	
10	B/O KALITHA	M	3.06KG	39	1	NVD	3	6	19	YES	
11	B/O KALA	F	2.5KG	38	2	LSCS	3	7	12	NO	
12	B/O PARIMALA	F	3.12KG	37	2	LSCS	2	7	20	YES	
13	B/O RAJESHWARI	M	2.93KG	38	3	NVD	2	5	17	NO	
14	B/O KULANTHAI THERESA	M	3.3KG	38	2	NVD	2	4	14	NO	
15	B/O ILAKYA	M	3.41KG	37	1	NVD	1	3	21	YES	
16	B/O DURGA	F	2.54KG	39	2	NVD	2	4	16	NO	74%
17	B/O LAKSHMI	M	2.6KG	39	3	LSCS	5	7	13	NO	
18	B/O KAVITHA	F	2.7KG	38	1	NVD	3	6	13	NO	
19	B/O GAJALAKSHMI	F	4.25KG	39	2	LSCS	2	5	11	NO	
20	B/O KOUSALYA STEPHEN	M	2.86KG	37	1	NVD	1	4	11	NO	
21	B/O NAGALAKSHMI	M	2.8KG	38	3	LSCS	3	4	11	NO	
22	B/O PRABHA	M	2.9KG	38	2	NVD	4	6	12	NO	
23	B/O MAHESHWARI	M	2.5KG	39	1	LSCS	5	7	14	NO	
24	B/O MEENA	M	2.75KG	37	1	LSCS	1	3	12	NO	
25	B/O SWAPNA	F	3.2KG	38	2	LSCS	2	5	19	YES	
26	B/O SUJATHA	F	2.9KG	39	2	LSCS	3	5	13	NO	
27	B/O MOHANA	M	2.7KG	37	2	NVD	3	7	11	NO	
28	B/O DHANALAKSHMI	M	2.68KG	37	1	NVD	1	3	17	NO	
29	B/O SHARMILA	F	2.5KG	38	2	NVD	2	6	13	NO	
30	B/O REKHA	M	2.93KG	39	3	NVD	3	5	18	YES	
31	B/O MEENA	M	2.88KG	38	2	NVD	2	6	17	NO	
32	B/O PRIYA	F	2.80KG	38	1	LSCS	1	4	12	NO	
33	B/O SARITHA	M	2.75KG	39	1	LSCS	1	3	19	YES	
34	B/O SIVARANJINI	F	2.9KG	39	1	LSCS	3	5	20	YES	
35	B/O CHARUMATHI	M	4KG	39	1	LSCS	1	4	11	NO	
36	B/O SUBADEVI	F	2.75KG	37	2	LSCS	2	5	11	NO	
37	B/O VIMALA	F	2.67KG	39	3	NVD	3	7	15	NO	

38	B/O NADHIYA	F	3KG	38	1	LSCS	1	3	13	YES	
39	B/O RANJANA	F	3.78KG	37	1	LSCS	2	5	13	NO	
40	B/O VIJAYALAKSHMI	F	2.76KG	39	1	NVD	2	6	12	NO	
41	B/O KAVIARASI	M	2.67KG	38	1	LSCS	3	7	13	NO	
42	B/O ANITHA	M	2.8KG	39	2	NVD	2	5	15	YES	
43	B/O ELAKIYARAJ	M	3.75KG	38	1	LSCS	3	5	14	NO	

CONTROLS

S.No.	NAME	SEX	BIRTH WEIGHT	GESTATIONAL AGE	PARITY	MODE OF DELIVERY	APGAR SCORE		THOMPSON SCORE	CONVULSIONS	DEVELOPMENT QUOTIENT
			(KG)	WEEKS			1 MIN	5MIN			
1	B/O RAJALAKSHMI	M	2.56	37	1	NVD	2	5	10	YES	93%
2	B/O MARIA	M	2.8	38	1	NVD	2	4	4	NO	87%
3	B/O MUTHULAKSHMI	F	2.66	37	2	LSCS	1	3	8	NO	90%
4	B/O NITHYA	M	3	39	1	NVD	1	4	9	NO	88%
5	B/O NAGESHWARI	F	2.75	38	3	LSCS	3	6	5	NO	86%
6	B/O NANDHINI	F	2.7	38	1	NVD	2	7	5	NO	87%
7	B/O SHALINIDEVI	F	2.6	39	3	LSCS	4	7	6	NO	86%
8	B/O SIVASANKARI	M	3.2	37	1	LSCS	3	6	8	NO	90%
9	B/O UMA	F	2.65	38	2	LSCS	2	6	7	NO	83%
10	B/O MANJU	F	2.72	39	2	NVD	3	6	7	NO	117%
11	B/O SARANYA	M	2.82	37	1	NVD	1	5	10	NO	50%
12	B/O GAYATHRI	F	2.88	37	1	LSCS	3	7	6	NO	88%
13	B/O BARGAVI	F	3.1	38	1	NVD	5	7	8	NO	105%
14	B/O SREEDEVI	F	4	39	2	LSCS	2	6	6	NO	92%
15	B/O CHANDRIKA	M	2.78	39	3	LSCS	1	5	10	NO	97%
16	B/O HEMA	F	2.8	37	1	NVD	6	7	4	NO	86%
17	B/O SHOBANA	M	2.6	38	1	NVD	5	7	5	YES	37%
18	B/O ARTHY	M	2.56	38	3	LSCS	4	6	6	NO	80%
19	B/O LAVANYA	F	2.63	39	2	NVD	5	7	7	NO	98%
20	B/O PRAGATHEE	F	2.58	37	3	LSCS	4	7	5	NO	90%
21	B/O MEGHA	M	2.55	37	2	LSCS	6	7	4	NO	65%
22	B/O KALPANA	F	3.5	39	2	NVD	3	5	9	NO	89%
23	B/O SHUBHA	M	2.9	38	1	LSCS	4	5	8	NO	58%
24	B/O KAVITHA	F	2.68	39	1	LSCS	5	7	5	NO	96%
25	B/O KANIMOZHI	M	2.99	37	1	NVD	6	7	4	NO	98%
26	B/O SATHYAPRIYA	M	2.87	37	2	NVD	3	0	6	NO	87%
27	B/O JULIE	F	2.78	38	3	LSCS	2	5	7	NO	88%

28	B/O AMRITA	F	2.74	39	1	LSCS	3	7	5	NO	87%
29	B/O ANUSHA	M	2.9	38	2	LSCS	5	6	4	NO	85%
30	B/O PRIYA	F	2.8	38	3	LSCS	4	5	7	NO	99%
31	B/O NIRANJANA	M	2.6	37	2	NVD	5	6	4	NO	102%
32	B/O ANITHA	F	2.7	39	2	NVD	5	7	5	NO	87%
33	B/O KALAISELVI	M	2.5	37	1	NVD	3	5	10	NO	89%
34	B/O SHASHIKALA	F	2.8	38	1	LSCS	4	6	8	NO	58%
35	B/O PRIYADARSHINI	M	3.1	39	2	NVD	5	7	6	NO	96%
36	B/O KALARANI	M	2.9	38	2	LSCS	3	4	9	YES	60%
37	B/O MAHALAKSHMI	F	2.78	39	1	NVD	5	6	7	NO	89%
38	B/O BRINDA	M	3.2	37	1	NVD	4	7	8	NO	94%
39	B/O MARIA JYOTHI	F	2.6	38	3	LSCS	6	7	5	NO	95%
40	B/O POORNIMA	F	3.5	39	1	NVD	5	6	5	NO	86%
41	B/O TARA	M	3	37	2	LSCS	6	7	8	NO	86%
42	B/O SUGUNA	F	3.2	39	1	LSCS	4	5	4	NO	90%
43	B/O APARNA	F	4	39	2	LSCS	4	7	4	YES	74%



ROLE OF THOMPSON SCORE IN PREDICTING NEURO DEVELOPMENTAL OUTCOME IN NEWBORNS.

Birth asphyxia is a condition of impaired gas exchange occurring during labour leading to progressive hypoxia associated with carbon dioxide retention and significant metabolic acidosis.It is an important cause of perinatal mortality and neurological morbidity,Recently new technologies have become available to determine cerebral damage more accurately and earlier in perinatal course.These include computerized tomography (CT),magnetic resonance imaging(MRI),cerebral function monitoring,cranial ultrasound and Doppler ultrasound of middle cerebral artery.These modalities are not available in many neonatal units ,and certainly not in developing countries.There is a need for a simple but accurate clinical method of predicting outcome.

AIM :To determine the ability of THOMPSON SCORE in newborn infant with HIE within 6 hrs of birth in predicting neurodevelopmental outcome at 9 months of age.

JUSTIFICATION OF STUDY:Simple non invasive clinical tool to select ideal candidate for neuro protective therapy,to do early intervention like physiotherapy,developmental assessment, occupational therapy,to minimize disability in future,to counsel the parents regarding prognosis early.

STUDY POPULATION:Child born with signs of HIE at birth are my study population.50 in each arm as exposed and unexposed group(including 10% lost to follow up)

Exposed-Thompson score more than 10

Unexposed-Thompson score equal or less than 10

Study period-9 months

Methodology-Term infants of 37 weeks of gestation or more are selected with clinical signs of HIE at birth.

INCLUSION CRITERIA-

BOTH 1 AND 2 SHOULD BE PRESENT

1)INFANTS≥37 WEEKS OF GESTATION ADMITTED IN NICUWITH ANY ONE OF FOLLOWING:

A)APGAR Score<5 at 10 minutes of birth

B)Continued need for resuscitation including endotracheal or mask ventilation at 10 minutes after birth.

C)Acidosis within 60 minutes of birth(umbilical cord,arterial,or cord PH<7)

D)Base deficit>16 mmol/lin umbilical cord or any blood sample within 60 minutes of birth.

2)Altered state of consciousness(lethargy,stupor or coma)atleast one of the following

A)Hypotonia

B)Abnormal reflexes(oculomotor and pupillary abnormality)

C)Absent or weak suck

D)Clinical seizures.

EXCLUSION CRITERIA:

1)Infants> 6hrs of age

2)Major congenital abnormality or syndromes that include brain dysgenesis.

Infants scored by THOMPSON SCORE within 6 hrs of birth and for 7 consecutive days.Infants followed up at 3,6,8 months of age.One cranial ultrasound should be done prior to discharge.Detailed neurological and development assessment will be done every 3rd month.

Table 1. Hypoxic ischaemic encephalopathy score.

Sign	Score 0	1	2	3
Tone	Normal	Hyper	Hypo	Flaccid
LOC	Normal	Hyper alert, stare	Lethargic	Comatose
Fits	None	Infreq $< 3\ d^{-1}$	Frequent>2/day	
Posture	Normal	Fisting, cycling	Strong, distal flexion	Decerebrate
Moro	Normal	Partial	Absent	
Grasp	Normal	Poor	Absent	
Suck	Normal	Poor	Absent ± bites	
Resp.	Normal	Hypervent	Brief apnoea	IPPV (apnoea)
Font'l	Normal	Full, not tense	Tense	
				Total score per day-

It is a clinical tool comprising of a set of clinical signs associated with CNS dysfunction.

It is used to assess status of a child following birth asphyxia.

In scoring system,a score of 0 is normal and maximum score is 22 which signifies worst possible status of HIE.

Infants scoring 1-10 are considered to have mild HIE,11-14 have moderate HIE,15-22 are considered to have severe HIE.

This is modified sarnat scoring system.

Infant neurological assessment should be conducted using DASI II by paediatrician.

Development activities screening inventory(DASI)II-It is designed for early detection of development delay with special focus on young children with language impairment whose cognitive abilities may not be accurately screened with a tool that requires the child to follow spoken instructions.DASI-II instructions may be either verbal or visual.There are 67 items which can be administered in one or two settings.

Description of scales

DASII scale is a point scale with items arranged in ascending order or age placement for both motor and mental scales.
The items in the two scales are classified into content clusters under different areas of development. There are five clusters of motor items and 10 clusters of mental items.

Motor clusters

I. Neck control
II. Body control
III. Locomotion I (Coordinated movements)
IV. Locomotion II (Skills)
V. Manipulation

Mental clusters

I. Cognizance (Visual)
II. Cognizance (Auditory)
III. Reaching, manipulation and exploring
IV. Memory
V. Social interaction and imitative behavior
VI. Language I (Vocabulary and comprehension)
VII.Understanding of relationship
VIII. Differentiation by use, shapes and movements
IX. Manual dexterity
The content clusters have great utility in clinical practice. They may be used in analyzing the child's performance in each area of development obtaining a profile of development with indication of areas of delay in development.
It helps to plan intervention strategy with referenceto child's strengths and weaknesses. It aids in effective counseling of parents for home based stimulation program.

Differential diagnosis with DASII

It is possible not only to identify delays and areas of delays with DASII but cluster analysis

can also help in differential diagnosis.

A Down's syndrome baby will have better motor than mental profile.A high functioning autistic child

will have almost normal motor profile and relatively low onmental but, especially low on language, social

interaction. He is likely to do better on memory,understanding of relationships or form boards.

A cerebral palsy child will score low onmotor items, imitative, skills but better on language

development, especially receptive language.He may do poorly on timed items, like

manipulation and manual dexterity clusters.A child with low stimulational and early

deprivation may show adequate score on motobut lower on mental clusters.

Thus, in trained hands, the DASII is a very comprehensive and effective tool often

considered the gold standard for developmentalassessment. It should be an integral part of any

developmental clinic where effective intervention is planned.

Points to Remember

• Developmental assessment should be an

integral part of NICU (Neonatal intensive

care unit)

• Developmental screening be done in all high risk infant as early as 3-6 months of

age

• DASII (Developmental assessment scales for Indian infants) is a very effective

comprehensive and useful tool which is standardized in Indian babies

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BWônf£ ¨ûXVm : ÏZkûRLs NêL SX UÚjÕYl©¬Ü AWÑ vPôu- UÚjÕYUû] ùNuû] - 6oo oo1.

TeÏ ùTßm úSôVô°«u ùTVo : YVÕ

TeÏ ùTßm úSôVô°«u Gi : Tô-]m : Bi ùTi

úSôVô°«u ®XôNm :

úSôVô° CRû] (▤) Ï±dLÜm :

úUúX Ï±l©hÓs[UÚjÕY Bn®u ®YWeLs G]dÏ ®[dLlThPÕ. GuàûPV NkúRLeLû[úLhLÜm, ARtLô] RÏkR ®[dLeLû[ùT\Üm YônlT°dLlThPÕ.

Sôu Gu ÏZkûRûV Ru²fûNVôLRôu TeúLtL AàU§d¡ú\u. GkR LôWQj§]ôúXô GkR LhPj§Ûm GkR NhP £dLÛdÏm EhTPôUp Gu ÏZkûRûV CqYôn®p CÚkÕ ®Xd¡d ùLôs[Xôm Guß A±kÕ ùLôiúPu.

CkR BnÜ NmTkRUôLÜm úUÛm CûR NôokR BnÜ úUtùLôsÞm úTôÕm CkR Bn®p TeÏùTßm UÚjÕYo Gu ÏZkûR«u UÚjÕY A±dûLLû[TôolTRtÏ Gu AàU§ úRûY«pûX G] A±kÕ ùLôs¡ú\u. Gu ÏZkûRûV Bn®p CÚkÕ ®X¡d ùLôiPôÛm CÕ ùTôÚkÕm G] A±¡ú\u.

CkR Bn®u êXm ¡ûPdÏm RLYpLû[Ùm, T¬úNôRû] Ø¥ÜLû[Ùm Utßm £¡fûN ùRôPoTô] RLYpLû[Ùm UÚjÕYo úUtùLôsÞm Bn®p TVuTÓj§d ùLôs[Üm AûR ©WÑ¬dLÜm Gu ØÝ U]ÕPu NmU§d¡ú\u.

CkR Bn®p TeÏ ùLôs[Jl×d ùLôs¡ú\u. Gu ÏZkûRdÏ ùLôÓdLlThP A±ÜûWL°uT¥ SPjÕ ùLôsYÕPu CkR BnûY úUtùLôsÞm UÚjÕY A¦dÏ EiûUÙPu CÚlúTu Gußm Eß§ A°d¡ú\u. Gu ÏZkûR«u EPp SXm Tô§dLlThPôúXô ApXÕ G§oTôWôR YZdLj§tÏ Uô\ô] úSôndÏ± ùRuThPôúXô EPú] ARû] UÚjÕY A¦dÏ ùR¬®lúTu G] Eß§ A°d¡ú\u.

CkR Bn®p Gu ÏZkûRdÏ RûX«p vúLu ùNnÕ ùLôs[Sôu ØÝ U]ÕPu NmU§d¡ú\u.

êuß UôReLÞdÏ JÚ Øû\ ÏZkûRûV UÚjÕY¬Pm Lôi©dL Sôu NmU§d¡uú\u.

TeúLtTY¬u ûLùVôlTm ..... CPm ..... úR§ .....

LhûP ®Wp (CkR T¥Ym T¥jÕ LôhPlThÓ ×¬kÕ ûLúWûL A°d¡ú\u)

TeúLtTY¬u ùTVo Utßm ®XôNm .....

BnYô[¬u ûLùVôlTm ..... CPm ..... úR§ .....

BnYô[¬u ùTVo .....

RLYp T¥Ym

êû[Tô§l× Utßm ARu A±Ï±Ls Es[ÏZkûRLû[G°Rp Utßm EPú] LiÓ©¥dL Rôm^u T¬úNôRû] Øû\ûV Tt± BWônRp

BWônf£«u úSôdLØm, TVuLÞm :

êû[Tô§l× Es[ÏZkûRLû[×§VØû\«p EPú] LiÓl©¥dLdá¥V Rôm^u T¬úNôRû] êXm AYoL°u êû[Y[of£ûV ®ûW®p LiÓ©¥jRp.

BnÜ SûPØû\Ls :

£¡fûN A°lTRtÏ HtTôÓ ùNnRp CqYôWônf£«u úSôdLUôÏm. EsúSôVô°L[ôL Es[êû[Tô§l× A±Ï±Ls Es[ÏZkûRLs CkR BWônf£«p úNojÕd ùLôs[lTÓYôoLs.

AkRWeL RuûU :

EeLs ÏZkûR«u UÚjÕY T§úYÓLs ªLÜm AkRWeLUôL ûYjÕd ùLôs[lTÓm Utßm ©\ UÚjÕYoLs / ®gOô²Ls / CkR Bn®u R²dûLVô[oLs ApXÕ BWônf£ BRWYô[oL°u ©W§ ¨§Ls B¡úVô¬Pm AûY ùY°lTÓjRlTÓm. CkR Bn®u Ø¥ÜLs A±®Vp Tj§¬dûLL°p T¬Ñ¬dLlTPXôm. B]ôp ùTVûW ùY°«ÓYRu êXm úSôVô°«u AûPVô[m LôhPlTP UôhPôoLs.

Bn®p EeLs TeúLt× Utßm EeLs E¬ûULs :

CkR Bn®p EeLs ÏZkûRL°u TeúLt× ØÝYÕm EeLÞûPV ®ÚlTjûR NôokRÕ. C§p ¿eLs TeúLtLúYô, UßdLúYô, Tô§«p ùY°úV¬PúYô ApXÕ Ï±l©hP úLs®LÞdÏ T§X°dL UßdLúYô EeLÞdÏ ØÝ E¬ûU EiÓ GlT¥ CÚkRôÛm EeLs ÏZkûR«u EPp ¨ûXdúLtT EeLs ÏZkûRdÏ ùTôÚjRUô] £¡fûN A°dLlTÓm RôeLs CÕ Ï±jÕ úYß ®TWeLs ùR¬kÕ ùLôs[®Úm©]ôp GeL°Pm úLhÓj ùR¬kÕ ùLôs[Xôm.

úUÛm ®TWeLs A±V ,rdLiP STûW AÔLÜm :

UÚ.T.ìTô

ThPúUtT¥l× UôQYo

ÏZkûRLs SX UÚjÕYm

AWÑ vPôu- UÚjÕY Lpí¬

ùNuû]

ùRôûXlúT£ Gi.994159312